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*Anderson, Geo. K., M.D.: *The Importance of Protein in Diet Therapy*, J. Am. Dietet. A. 21:436 (July-August) 1945.

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LEIOMYOSARCOMA OF THE STOMACH

Its Roentgenologic and Gastroscopic Diagnosis and Its Possible Relation to Pernicious Anemia

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LEIOMYOSARCOMA (leiomyoma malignum) is one of the rarest tumors of the stomach. It has been reported (7, 21) to comprise only 10 per cent of all gastric sarcomas. Since the frequency of sarcoma as compared to carcinoma of the stomach is said to be only 1:100, only one leiomyosarcoma should be expected to 1,000 cases of gastric carcinoma. Because we have observed 4 cases within a relatively short period of time, we feel that this statistical data may be misleading and that leiomyosarcoma may not be so rare as has been previously reported.

The diagnosis of this tumor is important because of its good surgical prognosis. The surgeon who may be inclined not to operate on large infiltrative carcinomas, must, nevertheless, consider the presence of a leiomyosarcoma which has a favorable prognosis, and should not refuse to give the patient a chance as long as this tumor cannot be excluded.

It would be most desirable to make the differential diagnosis before laparotomy. The 4 cases observed by us were all examined gastroscopically. Although gastroscopy did not lead to the exact diagnosis, the publication of gastroscopic observations made on these patients seems to be justified because they may aid in better evaluating the gastroscopic findings in the future.

We have collected a total of 94 cases of gastric leiomyosarcoma from the literature. Sixty-eight of these cases were published by Chaffin in 1938, and since then at least 26 additional reports have appeared.

PATHOLOGY

The differentiation of leiomysarcoma from benign leiomyoma is not easy. Transitions are to be expected theoretically. Cases have been described in which microscopically benign-looking tumors had metastasized and thereby unexpectedly behaved like malignant tumors. Borrmann comments on this fact by saying: "Thus we cannot always recognize whether or not certain cells are 'malignant.'" None of the 4 cases of our own can possibly be called a simple benign leiomyoma, inasmuch as they all show expansive growth not encountered in the simple benign myoma of the stomach.

Benign myoma of the stomach occurs frequently. Rieniets found 43 leiomyomas in 32 stomachs in 200 consecutive autopsies. These submucosal tumors are usually small and sharply circumscribed. Some may grow sub-

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seriously, others may grow toward the mucosa and finally protrude into the lumen of the stomach. They may become firmly fixed to the mucosa which often presents deep ulceration; however, the sharply limited, rounded character of the tumor, and the fact that it obviously belongs to the submucosal tissue, makes it possible to recognize it grossly at once. The evenly rounded character of the tumor effects a recession between its surface and the surrounding mucosa. The recession is crossed in a characteristic manner by mucosal folds, which, if found all around, prove that the tumor does not grow infiltratively toward the surroundings (19). Although transitional forms may occur, it may be stated that in none of our four tumors did the gastroscopic observation reveal the typical picture of submucosal benign myoma. Microscopically, the benign leiomyoma is composed of highly differentiated smooth muscle fibers.

Frequently, malignant leiomyomas will not form metastases for a long period of time, but they quickly break their natural boundaries, grow expansively and partly infiltratively and prove to be fatal. The infiltration never reaches the degree found in infiltrative carcinomas, and frequently a limiting capsule is still present. Occasionally "bridging folds" may be seen (see our Cases 2 and 3), but they are much less marked than in benign tumors and usually are present only in a small portion of the circumference of the tumor. Most leiomyosarcomas are probably malignant from the beginning on, although sometimes sudden rapid increase in size of a long quiescent growth, with ensuing cachexia, may be observed. Microscopically, the muscle cells of these tumors are not so fully differentiated and evenly built as they are in benign leiomyomas. The fusiform cells may be shorter or rounded and irregular in form and show many stages of differentiation of the smooth muscle cell, and mitotic figures in changing number may be found.

It is known that there are several gross forms of leiomyosarcoma (all of which were encountered in our own material). They may grow into the lumen of the stomach, and may then even become pedunculated (Case 3); they may expand within the gastric wall (Cases 1 and 4); or they may expand into the omentum or neighboring structures (Case 2). There is as little explanation for these different types of growth as there is for the different gross forms of gastric carcinoma. Ulceration of the mucosa covering the tumor is frequent in all forms.

The differential diagnosis between leiomyosarcoma and lymphosarcoma is particularly important, because the lymphosarcoma reacts so well to x-ray treatment (Buschke), while the leiomyosarcoma requires surgical treatment. In most cases these two forms of sarcomas should not be confused easily; the lymphosarcoma usually infiltrates the entire wall of the stomach, diffusely involving the entire organ (Bockus; Schindler, 15, 16), although sometimes solid circumscribed tumors may occur (13). The leiomyosarcoma grows more expansively, but less infiltratively. Exceptions may occur here too, so that microscopic examination of a biopsy specimen is finally the best method for institution of adequate therapy.

The differentiation between leiomyosarcoma and carcinoma is more difficult. It has been said that on palpation the leiomyosarcoma has a rubbery consistency as contrasted to the stony hard palpatory sensation caused by carcinoma, yet the gross differential diagnosis may be impossible.

Metastases were found in 15 per cent of our collected series. Cameron reports 20.5 per cent, but figures as high as 70 per cent appear in the older literature (Crohn). Metastases occur most frequently in the liver, even without evidence of tumor formation in the regional lymph nodes. They occur but rarely in the lungs and bones. The metastatic liver tumors may grow only slowly; Lemon and Broders have seen a patient live 6 years with a metastatic nodule in his liver.

CLINICAL FINDINGS

The three cardinal findings are: (1) gastrointestinal hemorrhage, leading to anemia; (2) epigastric or left upper quadrant pain; (3) upper abdominal mass. Each occurred in about 50 per cent of the collected cases. Gastrointestinal bleeding is frequently severe and recurrent. The abdominal pains vary from a

vague distress to a severe ulcer-like type of pain. The abdominal mass may sometimes fill the whole abdomen.

Nausea and vomiting do not occur frequently. Weight loss is usually only moderate in amount.

X-ray examination and gastroscopy should at least reveal the presence of a gastric tumor. The most important findings will be described in the histories of our own cases. The difficulty in making of the x-ray diagnosis will become apparent from our Cases 2 and 4.

In the collected series, x-ray examination revealed a filling defect in 59 per cent, an extrinsic mass was suspected in 18 per cent, stiffness of the gastric wall was described in 11 per cent, presence of ulcer niche without filling defect in 8 per cent; and in 4 per cent a negative gastrointestinal series was reported. In one case the correct diagnosis of leiomyosarcoma was made, and this case will be discussed later in detail.

There are but few gastroscopic reports. Twice (5, 9) the tumor was overlooked at gastroscopy. Lemon and Broders stated that postsurgical recurrence of multiple leiomyosarcoma was seen gastroscopically. The first gastroscopic description of a leiomyosarcoma was given by Schindler and Letendre in 1942 (18).

CASE REPORTS

CASE 1. The gastroscopic picture of this case has been previously described (18). L. Q., a white male, 26 years of age, was seen on October 22, 1940, at Billings Hospital, Chicago, (Unit No. 251259). For 3 years he had had a gnawing feeling in the epigastrium and attacks of weakness after exertion. Once he had fainted. He had been treated for pernicious anemia; the blood count showed red cells down to 2,800,000 and seemed to have responded to liver treatment.

Physical examination revealed no abnormalities except some pallor. Hemoglobin was 11.6 grams; red blood cells, 4,000,000; white blood cells, 9,000; gastric analysis showed 40 units of free hydrochloric acid after histamine.

November 4, 1940, x-ray examination of the stomach (Frederick Templeton) revealed the presence of large neoplastic masses: "These seemed to be benign but they were so large that one cannot be sure that they are not malignant. . . . Spectacular degree of polyposis."

November 6, 1940 gastroscopic examination (R. S.); report follows: "The whole stomach was seen and the picture was one which I have never seen before (Fig. 1). The angulus was seen and below it there

Fig. 1. Gastroscopic picture of leiomyosarcoma. Case 1. Tumor masses protruding from the posterior wall, covered by smooth soft mucosa. At 4 o'clock longitudinal ulceration. At the left side atrophic gastric mucosa with blood vessels.[1]

was a soft protruding mass which filled almost the entire antrum. The mucosa covering it showed many dark creases and folds. A dark hole in its upper portion seemed to be the way to the pylorus. Although this mass was unusually soft, I would not be able to exclude a malignant tumor from this picture alone. But then other protrusions were seen—5 along the posterior wall and 3 along the lesser curvature. Those of the posterior wall were large hemispherical protrusions, which, however, sloped gently toward the gastric wall. They all were covered by a smooth and soft mucosa, and no stiffness was observed. However, the highest of them, lying in the fornix, had a somewhat different appearance. Its surface was nodular and had a definitely polypoid character. The three protrusions of the lesser curvature were smaller, the two lower ones having about the size of a cherry and the highest the size of a plum. They were covered by smooth mucosa. Their elevation was partly so that a shadow was cast on the surrounding mucosa, but in other portions of the circumference there was a gradual sloping. The uppermost of these three formations contained many nodes of different size, and if we had seen this one alone we would not have been able to differentiate between a benign and a malignant adenoma. Its combination with many other tumors speaks for a benign polyposis. The mucosa surrounding the highest of these tumors and of the whole upper third of the stomach was grayish in color with branching blood vessels. It should be mentioned that in the groove between the highest and the next highest excrescence of the posterior wall there was a dark, red small depression which might or might not have been a small ulceration.

"Impression: (1) polyposis; (2) atrophic gastritis of fornix; (3) it is impossible to exclude malignant degeneration of the stalks of the nodes."

On November 11, 1940, an exploratory laparotomy was carried out (Dr. H. P. Jenkins). The

[1] Gastroscopic pictures drawn by Miss Eve Vermonde.

Fig. 2. Gross specimen. Case 1. Nodular mass in posterior wall and lesser curvature. Ulcer.

stomach was opened, extensive tumor masses within the wall of the stomach were found. A biopsy specimen of one of them was taken. Its microscopic examination revealed leiomyosarcoma. Thereupon a course of x-ray therapy was given with a total of 4,000 r's.

On February 21, 1941, a second operation was performed (Dr. Lester Dragstedt). No change was found in the size of the tumor masses as compared with that at the first operation; the x-ray irradiation had been ineffective. Gastrectomy, splenectomy, partial pancreatectomy, and esophagogastrostomy were carried out. The patient recovered. He received liver treatment and was doing well on September 6, 1941.

Gross specimen: The gross specimen consists of the entire stomach, spleen, and a small portion of the tail of the pancreas. The stomach contains a large, firm mass in the posterior wall and lesser curvature—10 by 6 by 6 centimeters (Fig. 2). It is nodular and firm but not hard. Its serosa is intact and the mucosa is also intact, except over one large protuberant node where it is ulcerated; the floor of the 1 centimeter-sized ulcer penetrates for at least 1.5 centimeters into the tumor mass. Over others of the nodes there are small areas of hemorrhage in the mucosa. The cut surface of the mass is firm, white, with a slight hemorrhagic discoloration at the center.

Microscopically (Figs. 3 and 4), the tumor mass is composed of round and spindle cells with a moderate amount of eosinophilic cytoplasm. There is a slight degree of anaplasia of the tumor cells. Mallory stain reveals only a very fine reticulum in the tumor mass. Phosphotungstic acid hematoxylin stain shows no myofibrils. There is very little difference between this specimen and the biopsy specimen taken before radiation therapy. Pathological diagnosis: leiomyosarcoma.

Summary. A 25 year old man had been treated under the diagnosis of pernicious anemia, but x-ray examination revealed large tumor masses of the stomach. Although malignant growth was considered, the diagnosis of polyposis was made. The same diagnosis was made at gastroscopy, although retrospectively it must be admitted that the picture

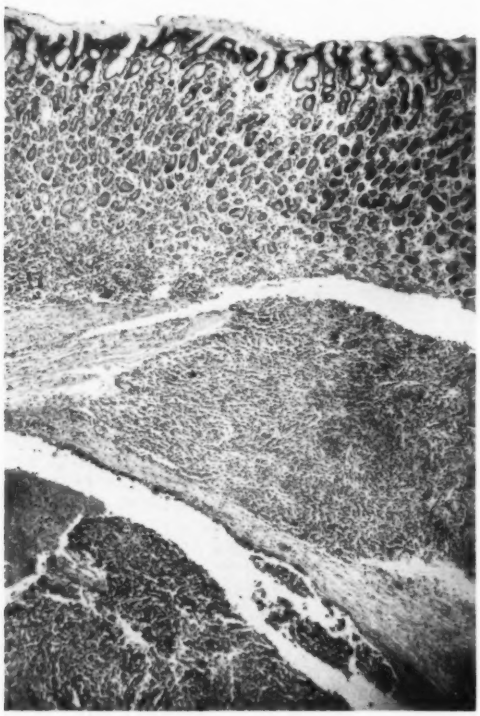

Fig. 3. Photomicrograph, Case 1. Survey. Section through rather normal gastric mucosa and adjacent tumor.

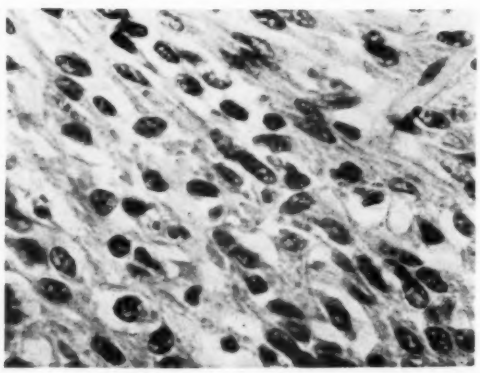

Fig. 4. Photomicrograph, Case 1. High power. Irregular sarcomatous tissue. Some typical smooth muscle cells.

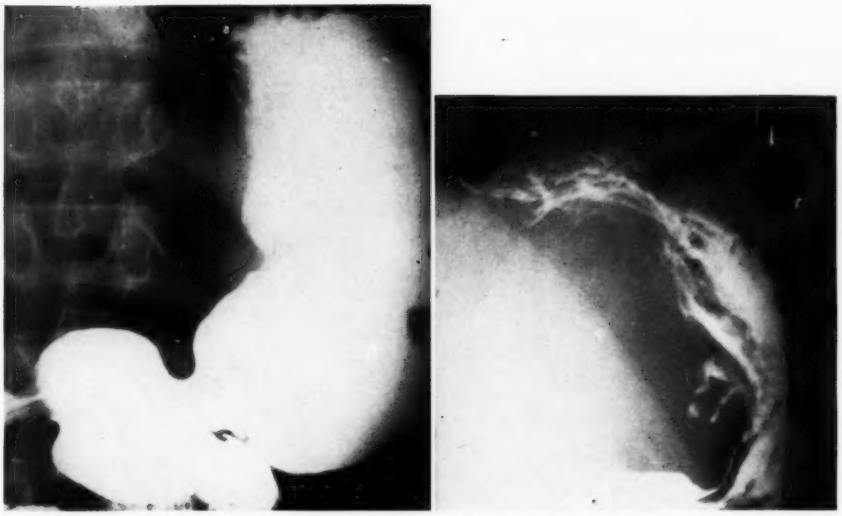

Fig. 5. Case 2. a, left, Roentgenogram taken before gastroscopy with complete filling: no pathology demonstrable. b, After gastroscopy—relief method: Shallow filling defect of lesser curvature with niche formation. Two fistulas extend into the depth of the tumor.

described in the gastroscopic protocol ("never seen before—"), was not consistent with the diagnosis of polyposis; the possibility of malignant tumor was considered. A biopsy specimen taken at an exploratory laparotomy revealed leiomyosarcoma. X-ray treatment was not effective. At a second laparotomy total gastrectomy with splenectomy amd partial pancreatectomy was carried out. The patient recovered.

CASE 2. A. S., 56 year old white male, No. 864521, entered Los Angeles County Hospital on December 21, 1943, with the history of melena which had occurred 24 hours before. In the afternoon of that day he suddenly felt sick, nauseated and vomited a cupful of dark blood. For 10 years he had vague abdominal distress, occurring hours after meals and relieved by food. There had been no recent weight loss.

Physical examination revealed a well developed, well nourished male. Slight pallor of the visible mucous membranes was present. There was mild epigastric tenderness, but no mass was felt. The hemoglobin was 56 per cent. Occult blood was found in the feces.

On January 26, 1944 the patient, after bed rest, dietary treatment, and transfusions, had recovered so much that x-ray examination seemed permissible.

First x-ray examination: The upper gastrointestinal series did not show anything abnormal (Fig. 5a) except spasticity of the duodenal bulb "consistent with early shallow ulcer." This diagnosis seemed clinically acceptable, and the patient was in such a good condition that his discharge was planned. He was seen by one of us in consultation, however, and advice for gastroscopy was given in order to determine, if possible, the true origin of the bleeding.

Gastroscopy was done on February 11, 1944, by Dr. David Niemitz and one of us (R. S.). (Fig. 6): "The instrument encountered resistance at first at the cardia, which was *suddenly* overcome and the instrument went into the depth of the stomach. The angulus and pylorus were in the two o'clock position, and a picture was even obtained in the three o'clock position. There was some dullness and formation of nodules in the lower anterior wall. As the instrument was withdrawn a hemispherical tumor entered the visual field at the six o'clock position (see Fig. 6). It was covered with smooth, very pale mucosa. No ulcer or necrosis was seen. Higher up the tumor was so close to the instrument that no detail could be made out. The tumor extended up to the cardia, was 8 centimeters in length. Impression: (1) tumor of greater curvature and posterior wall below the cardia. *Carcinoma is most likely; however, a benign tumor, especially myoma, may be present;* (2) distortion of the lower portion of the stomach; (3) mild hypertrophic gastritis of the lower portion of the stomach."

Because of the tumor seen a repeat x-ray examination was suggested.

Second x-ray: At this second examination, February 16, 1944, care was taken to examine the relief of the mucosa, and the patient received only one swallow of barium (Fig. 5b). "Two niche-like protrusions are seen on the posteromedial side of the stomach at the junction of the proximal and middle

Fig. 6. Gastroscopic picture. Case 2. In the upper third of the stomach a round *smooth* tumor was seen protruding from the greater curvature and posterior wall.

third. *These measure 2 centimeters in length and probably represent a perforation, which, in view of the gastroscopic findings, could be into a neoplasm.* The rugal pattern of the stomach is essentially normal (except in the area of the niches), but the cardiac end of the stomach appears to be displaced laterally and anteriorally by a soft mass. The findings are consistent with a perforated gastric ulcer with an adjacent inflammatory mass, or—less likely—perforation into a carcinoma."

As the gastroscopic diagnosis of a tumor seemed perfectly reliable, surgery was advised.

Operation was performed by Dr. H. Schiffbauer on February 24, 1944. A large tumor mass of the posterior wall was found. Total gastric resection proved feasible. The spleen was removed. The tumor was found to be firmly adherent to the tail of the pancreas so that resection of the tail of the pancreas became necessary. No metastases were found.

The patient survived the operation, a week later was in excellent condition, and made an uneventful recovery. He reported on September 20, 1944, that he felt fine. There was no recurrence of bleeding or of any gastrointestinal distress.

Gross pathology: The gross specimen is pictured in Figures 7 and 8. Figure 7 shows the resected spleen, tail of pancreas, and the posterior wall of the stomach containing an irregularly round tumor with node formation measuring 12 by 10 by 6.5 centimeters. In Figure 8 the upper half of the stomach has been opened across the anterior wall. In the posterior wall toward the lesser curvature there is an irregular ulcer 15 by 6 millimeters in size. Obviously this ulcer corresponds with the niche formation observed at the second x-ray examination (Fig. 5b), and it was missed gastroscopically because of its location in the well known "blind area" of the posterior wall (16). Close to its lateral margin a smooth, rounded protrusion can be seen. It is caused by a node of the tumor and was seen and diagnosed at the gastroscopic examination. In the picture of the gross specimen there are "bridging folds" at the

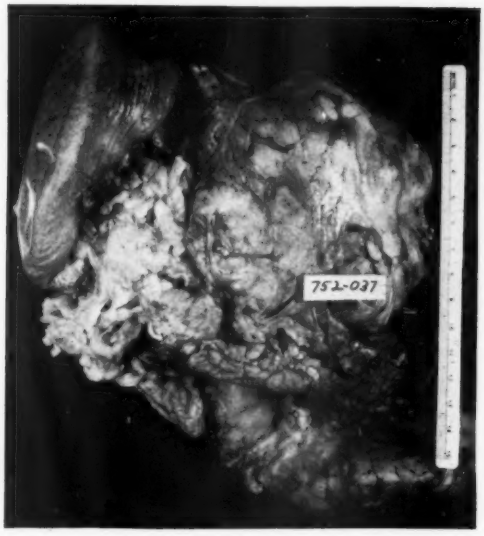

Fig. 7. Gross specimen. Case 2. Posterior surface. At left is the spleen, at right the expansively growing leiomyosarcoma of the upper portion of the stomach, beneath it (crossing the stomach) the tail of the pancreas.

lower pole of the tumor. Unfortunately, at gastroscopy the tumor bulged so much that the lower recess with these typical folds was not seen. The large tumor is found at the left side of the picture. It extended into the gastrocolic omentum and into the pancreas.

Microscopically, the typical picture of leiomyosarcoma is seen (Fig 9). At some places rather regular smooth muscle cells are found. But in other places the cells are irregular, only few nuclei still have the characteristic regular elongation with rounded edges of the normal nucleus of the smooth muscle cell. Most of them are oval or round, of various sizes, and mitoses are observed. Most portions of the gastric mucosa (except that of the ulcer area), of the muscularis mucosae, and even of the submucosa covering the tumor are perfectly normal.

Summary. A large leiomyosarcoma was found in a 56 year old male, which probably had developed over a period of about ten years and had caused only mild epigastric distress. Acute hemorrhage led to hospitalization. At the first x-ray examination the tumor was overlooked because no relief technique was used. Gastroscopy revealed the presence of the tumor, but the picture as seen was not exactly that of a carcinoma because the surface looked unusually smooth; however, it did not correspond with that of a benign myoma because the tumor extended diffusely toward the cardia. A second x-ray examination, with relief technique, revealed an ulcer niche. At surgery a leiomyosarcoma was found growing

Fig. 8. Gross specimen. Case 2. Anterior view. Upper two-thirds of stomach opened across the anterior wall. At the left side the huge tumor, at right upper corner the spleen. The inside of the stomach shows the ulcer, demonstrated by x-ray on Figure 5a, and the tumor protrusion seen at gastroscopy (Fig. 6).

expansively into the omentum and pancreas. Total gastrectomy with extirpation of the spleen and the tail of the pancreas led to cure, which, because of the good limitation of the tumor and the absence of metastasis, may be permanent.

CASE 3. W. B., a 60 year old white male, No. 104075, entered the White Memorial Hospital, Los Angeles, on July 11, 1943, complaining of increasing weakness for 1 year. For 8 months he had suffered from distress in the left epigastrium occurring 4 hours after meals, and which was promptly relieved by eating. About 2 months prior to entry he became dyspneic on mild exertion and noticed numbness and tingling in his extremities. Physical examination revealed marked pallor of the mucous membranes. The liver edge was felt just below the costal margin. No abdominal mass was felt and there was no tenderness. Hemoglobin was 6.3 grams, red blood cells, 900,000, color index 2.0, leucocytes, 3,900, reticulocytes, 0.5 per cent. Gastric analysis failed to reveal any free hydrochloric acid with the histamine test.

A tentative diagnosis of pernicious anemia was made. Treatment with parenteral liver extract was begun, and 6 days later the reticulocytes rose to 22 per cent. After 8 days the hemoglobin rose to 8.8

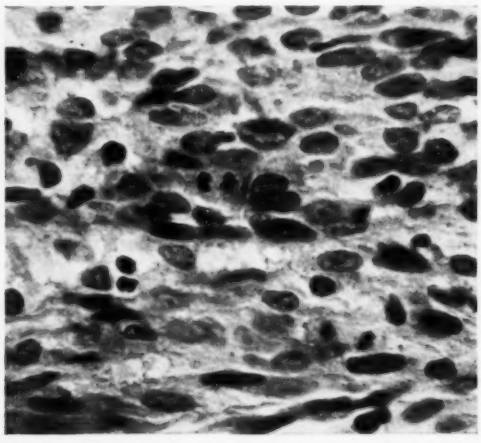

Fig. 9. High power photomicrograph, Case 2. Irregularly formed sarcomatous cells. Mitoses.

grams; red blood cells 1,960,000; and leucocytes, 8,500.

The first x-ray examination of the stomach was done on July 15, 1943 (Dr. Stilson) with the following report: "The stomach is of average tone. The major portion of its lumen is regular and flexible. The cardiac end of the stomach, however, on the film appeared rather peculiar, and it is evident that the stomach empties rapidly. . . . Probable neoplasm of the cardiac end of the stomach."

The second x-ray examination was carried out by Dr. W. L. Stilson on July 19, 1944, after the first gastroscopy. The report read: "Now there are demonstrated definitely, fluoroscopically, and on the films, extensive filling defects involving the proximal portion of the stomach, except the extreme cardia, and extending for a distance of approximately 9 centimeters. The lesion apparently arises about 3 centimeters distal to the cardia."

The x-ray pictures are partly rendered in Figures 10 and 11. In Figure 10 only the colon is filled with contrast meal, but the stomach is empty. Here a tumor can be seen very well as a shadow within the air bubble of the stomach. Figure 11 demonstrates the large filling defect in the barium-filled stomach. One should notice that no central crater is definitely visible, though the barium accumulation at the lesser curvature side of the tumor may be interpreted thus.

Two gastroscopic examinations were carried out.

First gastroscopy (O.A.B.) on July 18, 1944: "The pyloric end of the stomach was well seen and several peristaltic waves could be seen running down to the pylorus, the entire circumference of which came into view. Just above the angulus along the lesser curvature there were 2 or 3 rather prominent folds which seemed to be somewhat redder than the surrounding mucosa, which was extremely pale. About 5 or 6

Fig. 10. Case 3. A coil of the colon is filled. The stomach is empty. The tumor is outlined toward the dark background of the gastric air bubble.

Fig. 11. Case 3. Stomach filled. Trendelenburg position. Large filling defect.

centimeters above the angulus on the anterior wall, extending down to the greater curvature, a well defined mass could be seen. This mass was very red and succulent in appearance in contrast with the extremely pale surrounding mucosa, and there seemed to be several finger-like processes . . . When the instrument was withdrawn the large red mass came in contact with the objective, and it was impossible to see its uppermost portions. Along the posterior wall and greater curvature, in the lower part of depth II, blood could be seen lying between the rugal folds, but no point of active hemorrhage could be seen. In all portions of the stomach which were observed . . . the mucosa was extremely pale, almost to the point of whiteness.

"Impression: (1) carcinoma of the stomach involving the anterior wall and greater curvature of the upper and midportions of the stomach. (It was impossible to visualize the margins of this tumor mass, and hence I cannot be certain that it does not extend all the way up to the cardia); (2) no gastritis seen."

Second gastroscopy (O.A.B. and R.S.) on July 20, 1943: "Immediately with the objective turned to nine o'clock extensive pathological changes were seen. A stiff protruding area bulged into the cavity of the stomach from its anterior wall, involving the greater curvature also. At its deepest point there was a dark red protuberance, and to both sides of this protuberance was a less dark wall surrounding the stiff area. This wall hung over in a mushroom-like fashion and pale pink, soft normal mucosa was submerged beneath the margins of the mushroom-like wall. On the top of the stiff elevation there was extensive white necrosis or ulceration . . . When the instrument was withdrawn the infiltrated area came close to the objective. The wall, however, could be followed all around the lesion. It became much thinner in the upper portions of the stomach, but remained sharply limited from the surrounding pale mucosa to which its dark color formed a decided contrast. In this pale mucosa no sign of atrophy, no thinning, and no blood vessels were seen. Toward the upper edge of the wall several *mucosal folds converged, one of them running up to the wall in a manner usually only seen in submucosal tumors* (see Fig. 12). There was no infiltration. The upper limit of the wall was found to lie 6 centimeters below the cardia. Impression: (1) large carcinoma of the anterior wall and greater curvature of the body of the stomach. (This is most likely a Type II carcinoma according to the classification of Borrmann. These Type II carcinomas usually give an excellent surgical prognosis.) (2) No gastritis visible."

On July 23, 1944, a gastric resection with anterior Pólya anastomosis was performed, leaving only a small amount of the subcardial portion of the stomach (Dr. George Thomason). The patient recovered.

The gross specimen contained a pedunculated tumor of the cardiac end of the stomach. This pedunculation is not well demonstrated on the picture of the gross specimen (Fig. 13), which demonstrates more the gastroscopic aspect. The tumor was 6 centimeters in diameter. Its surface was rough, irregular, and contained three large ulcerated areas. A Type I Borrmann carcinoma was diagnosed at gross inspection.

Microscopically, the tumor consists of smooth muscle tissue. The cells are partly regular and well

Fig. 12. Gastroscopic picture, Case 3. At the left lower margin the fold of the cardia is seen. It is separated by normal mucosa from the upper edge of a tumor. The protruding tumor has a nodular wall and contains a large ulceration. Note especially the one "bridging fold" running from the normal mucosa up to the tumor wall because of its diagnostic significance.

Fig. 13. Gross specimen, Case 3. At the right side of the large tumor there is extensive ulceration. The pedunculation does not show.

differentiated, partly irregular in form and without complete differentiation (Fig. 14). Scattered between the solid tumor masses are nests of plasma cells and macrophages. Where the tumor pierces the mucosa, there is no sharp capsule. The neighboring mucosa shows some cysts at the bottom of the glands.

The mucosa of the anterior wall and lesser curvature distant from the tumor shows mild but definite changes. The interstitium between the long body glands contains few cells, mostly plasma cells and fibroblasts. The muscularis mucosae itself is split up. Between the muscle fibers are inflammatory cells. Most of the body glands are normal, but some pits are proliferating toward the depth, and at a few places metaplasia into an intestinal type of epithelium is seen. The surface epithelium shows mild but definite proliferation, and between the pits there is some slight edema. Thus there is a mild but definite atrophic gastritis present. (It may be said here that this picture, in our opinion, is compatible with the diagnosis of pernicious anemia. It is of interest, furthermore, that this mild degree of atrophic gastritis was not recognized at two gastroscopies).

Six months later the patient complained of swelling of the legs and of anorexia, but under continued liver treatment the distress disappeared. The blood picture remained normal. However, the patient was constantly treated with liver injections.

A third gastroscopy was undertaken on July 23, 1944 (O.A.B.): "The gastroscope entered the jejunum, no tumor was seen. The gastric mucosa looked pretty normal, but toward the cardia there was some thinning with blood vessels—atrophic gastrititis—not seen at the previous gastroscopies."

The patient was last seen in March 1945, at which time he felt quite well. Repeated x-ray examinations have failed to reveal any recurrence of the tumor. There was immediate emptying of the stomach stump.

Summary. In a 60 year old man the fully developed picture of pernicious anemia was found: macrocytic anemia with a color index of 2, typical reticulocyte response to liver therapy and histamine proved anacidity. X-ray examination and gastroscopy revealed a circumscribed tumor of the upper third of the stomach without gastritis. In the gross

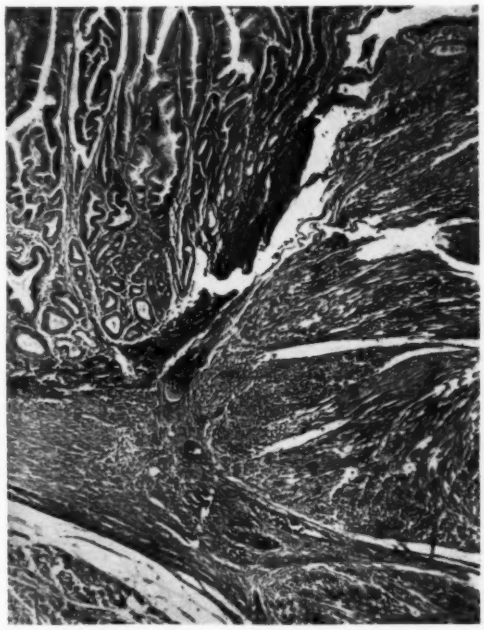

Fig. 14. Photomicrograph, Case 3. The gastric mucosa contains cysts and "cork-screw" glands,—first signs of atrophy. The myomatous tumor at its break-through through the stomach wall has no capsule.

Fig. 15. Case 4. Roentgenogram interpreted as normal. However, in the fornix a contour and a fleck are seen which may be interpreted as the outline and central ulcer of the tumor.

resected specimen this tumor was found to be a pedunculated one, but only at microscopic examination was the diagnosis of leiomyosarcoma made. Retrospectively, it must be admitted that the second gastroscopic examination (Fig. 12) had revealed a feature which should have been considered as almost incompatible with the picture of gastric carcinoma; namely, the presence of a "bridging fold," as described previously (19) as characteristic of submucosal tumor. The very large ulceration and the high dark red wall surrounding the ulceration reminded one so much of the frequently observed pictures of gastric carcinoma that the importance of this one fold for the correct diagnosis was underestimated, although the gastroscopic protocol stated the presence of such a bridging fold, "usually only seen in submucosal tumors."

The tumor was removed by extensive resection and the patient is living now in satisfactory condition. Of special interest is the blood picture obtained in this case. It will be discussed later.

Case 4. E. T., a 46 year old Ethiopian female, entered the Los Angeles County Hospital on January 16, 1941. One year before admission she had had hematemesis, followed by occasional passage of black stools. She noticed increasing constipation and a weight loss of 60 pounds. Three weeks before entry she became weaker and dyspneic. Repeated melena was observed. Twelve days before admission she vomited one pint of dark blood. She had had only a little epigastric distress.

Physical examination revealed an obese colored woman, with pallor of mucous membranes, râles at the base of the left lung, and a systolic murmur over the mitral valve. On palpation of the abdomen no masses were felt. Gastric analysis revealed 85 units of free hydrochloric acid after histamine.

X-ray examination, February, 20, 1941, revealed the following: Esophagus and stomach did not reveal any abnormalities. There was a normal 6 hour progress. The duodenal bulb was smooth. The hemoglobin, which was 15 per cent on entry, was brought up to 70 per cent after numerous transfusions. On March 19, 1941, the patient was discharged with the diagnosis of gastrointestinal hemorrhage of unknown etiology.

She re-entered the hospital on June 28, 1941, because of melena. The hemoglobin was down to 18 per cent. On July 14, 1941, x-ray examination was again undertaken: "Normal six hour progress. Esophagus and stomach essentially negative. The duodenal bulb is small, but showed smooth outlines fluoroscopically. No tenderness, irritability or spasticity."

Gastroscopy (H.L.T.) was carried out July 23, 1941 and the report follows: "Pyloric end of stomach normal in color and configuration, except that there were multiple small pigmented hemorrhagic areas. In the proximal portion of the body there was a large necrotic ulcer with a fungating hyperplastic edematous margin, typical of carcinoma. The high position and large size of the lesion makes its operability questionable. In view of the otherwise good general condition of the patient, surgical exploration is probably advisable."

X-ray films were taken again on July 25, 1941. Then a "constant filling defect of the cardiac end of the stomach on the greater curvature side, consistent with a polypoid neoplasm, probably carcinoma" was found. (If, however, Figure 16 of this x-ray examination is studied, the conclusion may be drawn that there is a tumor of the cardiac end of the stomach with a central ulcer. The significance of this picture will be discussed later.)

On July 31, 1941, total gastrectomy with splenectomy and partial pancreatectomy was carried out (Dr. Harlan Shoemaker). The patient died postoperatively on August 5, 1941, from massive pulmonary atelectasis.

The gross specimen consisted of the excised stomach which contained in the upper posterior wall a cartilaginous-looking mass, measuring 15 by 11 by 4.5 centimeters, with a large mucosal ulcer of its central portion. The tumor had grown expansively beneath the mucosa and extended to the serosa, forming there a knobby projection.

Microscopically, there are intertwining bands of elongated spindle-shaped cells. Few mitotic figures are seen. The regional lymph nodes do not contain

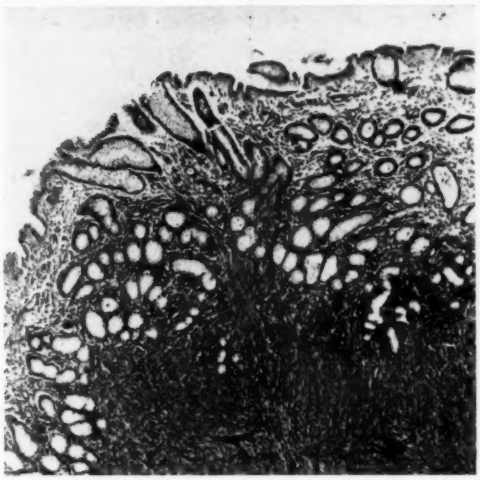

Fig. 16. Case 4. The diffusely infiltrative leiomyosarcoma has grown destructively into the gastric mucosa. Signs of atrophy.

any tumor cells. Figure 17 shows that the tumor invades and destroys the mucosa which contains only remnants of glands. Some of these may still be seen within the tumor tissue, some show cystic dilatation.

An autopsy was performed by Dr. L. K. Andersen. Massive atelectasis of the lungs was found. In the liver there was a firm nodule, 2 centimeters in diameter, on the posterior surface of the left lobe. Microscopically it proved to be a leiomyosarcoma metastasis (Fig. 17) without capsule.

Summary. A 46 year old woman had had severe attacks of hematemesis and melena for over a year. The source of the bleeding was not found after the first admission and would have been overlooked at the second admission without gastroscopy. With this method an ulcerated tumor of the upper portion of the stomach was seen and interpreted as a carcinoma. Surgery revealed an intramural leiomyosarcoma. Total gastrectomy with splenectomy and partial pancreatectomy was performed. The patient died from massive pulmonary atelectasis. On autopsy one small metastatic node in the liver was found.

DISCUSSION

A brief discussion of the x-ray diagnosis, gastroscopic diagnosis, relationship to pernicious anemia, and therapy of leiomyosarcoma of the stomach follows.

X-ray diagnosis. In our material the diagnosis of a gastric tumor was missed at one x-ray examination in Case 2 and at two x-ray examinations in Case 4. In these 2 cases the presence of a gastric tumor was found at gastroscopy. This rather poor result can obviously be improved. In both cases the tumor could be demonstrated at a repeat x-ray examination when the proper technique was used. These 2 cases prove again the fact that the method of filling the stomach completely with barium suspension and then taking films is unsatisfactory. It must be replaced routinely by the relief method (22). With this method the relief of the stomach is studied and much finer lesions than those found in Cases 2 and 4 will not be overlooked.

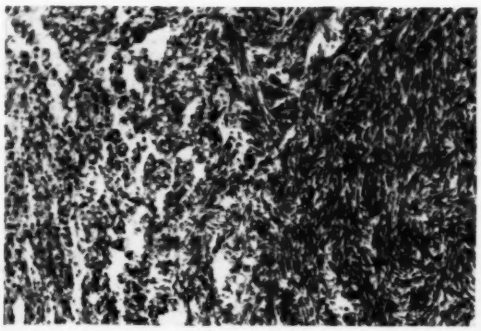

Fig. 17. Case 4. Photomicrograph showing liver metastasis. At left liver tissue. At right leiomyosarcoma-tissue without capsule.

The diagnosis of benign submucosal tumor at x-ray examination can be dared if a sharply defined round filling defect with a central niche is noted. The central niche is characteristic of the central ulceration so frequently found in these tumors. However, in leiomyosarcoma it may be more difficult to state that this tumor originates from beneath the mucosa; i. e., from the submucosa or muscularis propria. A case report published by Chaffin, however, shows how astonishingly correct diagnoses become possible if proper technique and deliberate interpretation are used. The x-ray examination in that case was carried out by Dr. D. R. Laing of Pasadena, and the x-ray protocol (May 28, 1936) read:

"The stomach is somewhat hypertonic. Near the junction of the distal and middle thirds of the stomach is an area approximately 5.5 centimeters in diameter, which is not covered with barium except for an area 2 centimeters in diameter in its approximate center. There, a few radiating lines extend from this center pocket of barium to the proliferation

of the rounded lesion. The stomach was very pliable. Peristaltic waves moved over very freely, and were only lessened in this region to the extent that the lesion impinged on the respective curvatures. The rugal pattern was intact, except in the area occupied by the lesion. The center of the lesion could be emptied of its barium by palpation. There was no tenderness in this lesion. The duodenal bulb filled readily and smoothly. The findings are suggestive of leiomyoma with central necrosis, which may be due to sarcomatous degeneration. The possibilities of localized hypertrophic gastric mucosa or a large polyp with central ulceration or umbilication must also be considered."

Here proper interpretation had lead to the correct diagnosis of a submucosal tumor. The central ulceration seen was interpreted in favor of sarcomatous degeneration. This is not correct. Perfectly benign submucosal tumors of every kind, even lipomas, may have similar central ulceration. In this case, however, definite leiomyosarcoma was found microscopically, and the fact remains that the roentgenologist had stated correctly that a malignant tumor of the stomach had originated from the submucosal layers.

If we review critically the x-ray protocols of our 4 cases, then we may say that in Case 1 probably the correct diagnosis of a tumor originating submucosally was impossible. Large neoplastic masses were seen, they appeared benign, but malignant growth could not be excluded. However, at the examination of the excised gross specimen an ulcer was found, and the floor of this ulcer penetrated for at least 1.5 centimeters into the tumor mass. This indicates a kind of fistula formation. Such a fistula might have been seen at x-ray examination. In carcinoma this feature is observed rarely, if ever.

Case 2 shows that this sign may be demonstrated at the x-ray examination of leiomyosarcoma. At the second x-ray examination the picture rendered in Figure 5b was obtained. A shallow filling defect is seen with an ulcer niche formation. Two fistulas extend into the depth. Each of these fistulas has a length of 2 centimeters. They were described well in the x-ray protocol. In consideration of a similar picture in the gross specimen of Case 1 we conclude that filling defect with central niche and fistulas at x-ray examination is rather characteristic of leiomyosarcoma.

In Case 3 the tumor was at first seen best as a round shadow within the gastric air bubble. Later a round filling defect within the barium was seen. The diagnosis of submucosal tumor was impossible at x-ray examination because the tumor protruded into the mucosa and was pedunculated. We do not believe that at x ray examination the differentiation from carcinoma in this form of leiomyosarcoma is possible.

In Case 4 two x-ray examinations had failed to reveal the tumor. After gastroscopy at a third x-ray examination: "Polypoid neoplasm, probably carcinoma" was found. But, if we look at this picture (Fig. 15) then we see a central niche within a tumor of the fornix, and this central small crater may have suggested perhaps presence of a submucosal tumor.

Thus we come to the conclusion that in 3 of our 4 cases the x-ray diagnosis of a submucosal tumor would not have been entirely impossible. It must be admitted that in some cases (as in our Case 3) the differentiation from carcinoma at x-ray is impossible, but the x-ray syndrome of filling defect, plus central niche, plus fistulas, should be considered as highly suggestive of leiomyosarcoma.

Gastroscopic diagnosis. In none of the 4 cases was the correct diagnosis made at gastroscopy, but in 2 of the cases (Cases 2 and 3) features were described in the gastroscopic protocols which had a certain relationship to submucosal tumors, and this relationship had been stated.

If we analyze the gastroscopic pictures of the 4 cases, we find that in Case 1 the gastroscopic protocol offers no foundation for the final diagnosis of "polyposis." The gastroscopic findings correspond with every feature later found in the gross specimen. This gross specimen has no similarity to the well known picture of gastric polyposis. The protocol states that in the antrum a "soft, protruding mass" was seen. Other large hemispherical protrusions were described, which "sloped gently toward the gastric wall." The elevation of other small protrusions was "partly so that a shadow was cast on the surrounding mucosa, but in other portions of the circumference there was a gradual sloping." This description does not

fit with any picture of carcinoma, neither does it correspond with the known pictures of lymphosarcoma. It certainly should not have been interpreted as polyposis. We believe that the appearance of the antrum alone would have permitted the diagnosis of a sarcoma.

In Case 2 the correct diagnosis of a tumor was made. It was then stated that: "Carcinoma is most likely; however, a benign tumor, especially myoma, may be present." The latter tumor was considered because of the smoothness and roundness of the tumor seen. The consideration of carcinoma and of myoma came pretty close to the truth, and one cannot consider this diagnosis as entirely wrong. The gross specimen showed "bridging folds" at the lower pole of the protrusion, but these folds, the observation of which should have established the diagnosis of a submucosal tumor, were not seen at gastroscopy. It seems that these folds usually are numerous and present at all sides of a benign submucosal tumor, but they are only occasionally seen if the submucosal tumor starts to grow expansively and infiltratively.

Only one such fold was noticed in Case 3 (Fig. 12). Its presence should have forced the observer into the correct diagnosis in spite of his unwillingness to assume another case of leiomyosarcoma. We quote here the decisive sentence of the protocol in order to show how reliable such apparently minor gastroscopic signs are: "toward the upper edge of the wall several mucosal folds converged, one of them running up to the wall in a manner usually seen only in submucosal tumors."

In Case 4 the gastroscopic appearance was that of a carcinoma, and retrospective analysis reveals no sign which could have been interpreted as characteristic for a submucosal tumor.

Thus, we come to the conclusion that in 3 cases (1, 2 and 4) the x-ray diagnosis would not have been impossible, and that in 3 cases (1, 2 and 3) the correct gastroscopic diagnosis should have been made. The preoperative diagnosis of leiomyosarcoma of the stomach is in the realm of possibility.

Relationship between leiomyosarcoma and pernicious anemia. The frequency of benign adenomas in pernicious anemia is well known (Brown; Schindler, 17). More and more the opinion gains ground that carcinoma develops secondarily to pernicious anemia more frequently than should be expected. However, no such relationship is known between pernicious anemia and tumors of muscular tissue.

In our material twice a pernicious anemia was diagnosed (Cases 1 and 3). This diagnosis was obviously wrong in Case 1 in which free hydrochloric acid was found at the histamine test. In Case 3 the clinical picture was that of pernicious anemia. The hemoglobin was 6.3 grams, with a red count of only 900,000. The color index was 2.0. The white count was 3,900. There was 0.5 per cent of reticulocytes. After liver therapy there was a typical response, the reticulocyte count went up to 22 per cent. There was no free hydrochloric acid in the gastric contents at histamine test.—The gastric mucosa did not show any sign of inflammation at gastroscopy, but by microscopic examination mild but definite atrophic gastritis was found. Schindler and Serby (20) described cases of untreated pernicious anemia in which only partial atrophic gastritis was seen and one case in which no atrophy at all was seen, but only superficial gastritis. The conclusion must be drawn that pernicious anemia is not necessarily accompanied by severe or complete atrophy, but that mild inflammation may be present as well.—In this Case 3 everything speaks in favor of pernicious anemia being present.

Relationship between pernicious anemia and the gastric muscularis propria is known to exist. Koch described 3 cases of hypertrophy of the pyloric musculature in pernicious anemia. Mayeda described enormous thickening of the muscularis propria, increasing from the cardia to the pylorus, in a case of pernicious anemia. It is true that in cases of malignant tumor of the stomach macrocytic anemia has been observed, but in all such cases the question remains open, whether or not the macrocytic anemia preceded the tumor formation. Although we cannot exclude the possibility of a macrocytic anemia caused by the leiomyosarcoma of our Case 3, we want to suggest the possibility of the reverse sequence, namely, pernicious anemia leading to formation of leiomyosarcoma.

Treatment. The gross and microscopic observation in Case 1 shows that x-ray treatment of gastric leiomyosarcoma is ineffective.

Surgery, however, proved to be eminently satisfactory. In one case (Case 3) extensive gastric resection was carried out. In the 3 other cases total gastrectomy with splenectomy and pancreatectomy was performed. Only one patient died postoperatively, (Case 4) and this death was not due to abdominal catastrophe, but to massive pulmonary atelectasis. Three patients survived the enormous procedure and seemed to be cured permanently. It is remarkable that these operations were performed by four different surgeons in three different institutions. Certainly surgery was in extraordinarily competent hands in all cases, and there is no doubt that great progress has been made with the technique of such procedures as total gastrectomy and partial gastrectomy. Yet, one may consider the possibilities that the vitality of patients with leiomyosarcoma may not be so affected as it is usually in carcinoma. In leiomyosarcoma the surgeon cannot be easily too courageous. The excellent results obtained in our series justify the attempt to remove even the largest tumors.

SUMMARY

1. Four cases of leiomyosarcoma have been described.

2. The possibilities of the roentgenologic and gastroscopic diagnosis of this tumor have been discussed, its possible relationship to pernicious anemia has been considered, and the excellent results of surgical treatment have been described.

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COMPOSITE FREE GRAFTS OF SKIN AND CARTILAGE FROM THE EAR

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FREE grafts, consisting of two surfaces of skin with cartilage between, can be considered for the replacement of tissue lost from areas such as the nostril border and tip and columella. These defects can be corrected in one procedure with the best resulting appearance of any method used; there is minimal deformity of the donor site and the use of bulk flaps is avoided. The ear can be repaired with a local flap or by burying the open ear under a direct scalp flap from behind, and freeing it and grafting the defect 2 to 3 weeks later.

The procedure is useful for tissue losses from burns, gunshot and shell fragment wounds, as well as other traumatic or operative losses. It is necessary that there be a

This work has been done at Valley Forge General Hospital in association with Major Carl E. Lischer, Major Parke Scarborough, Captain Bowdoin Davis, Captain Andrew Moore, and Captain Joseph Murray.

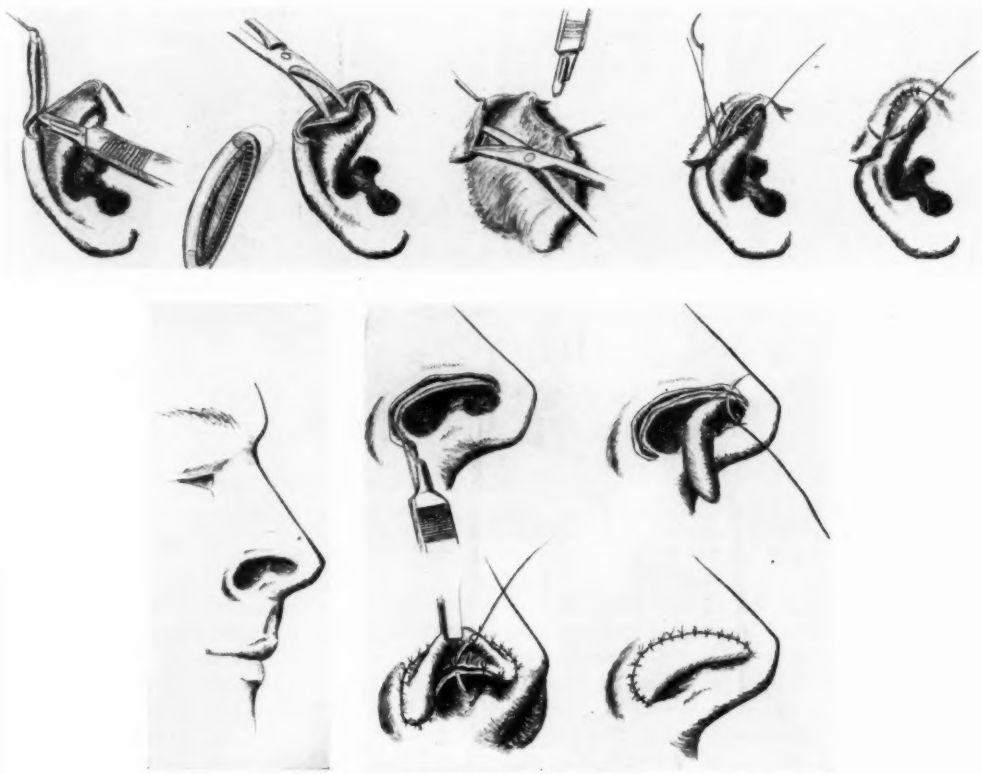

Fig. 1. Illustrating the steps in repair of nostril border with composite free grafts of skin and cartilage. Drawing by T/5 David G. Parsons.

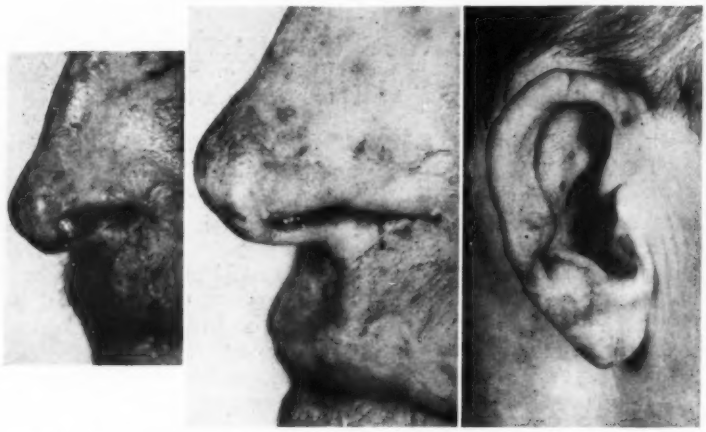

Fig. 2. Complete restoration of ala in single operation with composite free graft of skin and cartilage. Ear border already deformed by being shot through, used for ala before repair of ear with direct scalp flap. Flap detached 3 weeks later.

Fig. 3. Restoration of columella, tip, and ala in a single operation by use of composite free graft of skin and cartilage. Notching of upper and lower lips has been corrected.

satisfactory minute blood supply in the recipient area, and the defect has to be opened widely and deeply over a sufficient area. This procedure creates a larger defect to be filled than the original defect.

The size of replacement tissue, of course, is limited. So far, the whole columella, tip, and one border of the nose have been put in at one operation, also nostril borders on two sides. A great bulk of tissue cannot be transplanted as a free graft; the maximum at present has been about 1 centimeter in width, length has not been important. The amount of available ear structure is also a determining factor, the part of the border containing cartilage being used. (In some instances, the ear border is already deformed and has to be repaired anyway so that no extra operation

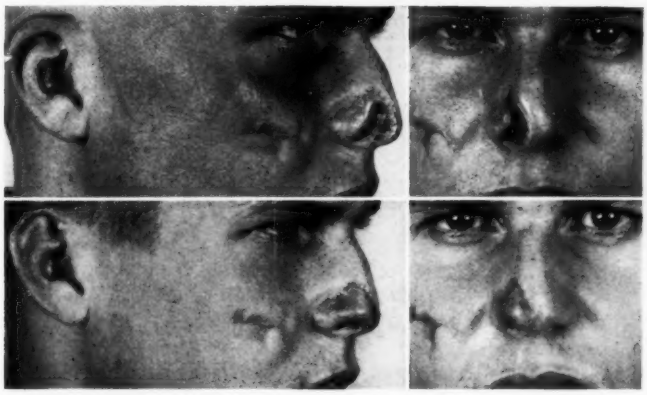

Fig. 4. Large replacement of nostril defect by use of free composite graft of skin and cartilage in a single operation. Minimal ear deformity with scalp flap restoration.

necessary. The desired graft is taken off for the nostril when the ear is repaired. In severe burns, when both ears are largely destroyed, the source is lost.) At operation the defect is prepared so that the area has a good minute blood supply. The graft is cut to pattern from a suitable portion of the ear, in a region where cartilage presents just under the skin. Care is taken not to separate skin from cartilage. The crus of the helix can be utilized.

The graft is sewed accurately in place with fine sutures along all edges, with one or two deep ones at the start.

The nostril is packed and a firm pressure dressing applied. The graft may become blue and discolored and even blister, and careful attention and protection are required in its management.

Small areas of flat cartilage with overlying skin can also probably be done, but enough observations have not been made to report this variation. This graft is taken from behind the ear and the skin is cut larger than the cartilage so that it can spread out and pick up a blood supply. These grafts necessarily have to be small, and the skin over the cartilage probably survives because of a lateral blood supply coming in through the edges rather than by a supply through the cartilage.

SUMMARY

Sections of the border of the ear containing two surfaces of skin with cartilage in between have been successfully transplanted as free grafts, and defects of the nostril border tip and columella have been repaired satisfactorily in a single operation.

SUBCUTANEOUS HEPARIN IN THE PITKIN MENSTRUUM FOR THE TREATMENT OF EXPERIMENTAL HUMAN FROSTBITE

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WHILE numerous reports[7] have been published concerning the morphologic changes that occur in frostbite, the literature concerning the functional pathology is scarce. Green's excellent studies of the pathologic changes occurring in experimental frostbite pointed the way for detailed investigation of the physiologic changes occurring in this lesion. The use of the fluorescein test (3,4) was a medium through which the sequence of events could be observed in tissues exposed to severe cold. In this test small amounts of fluorescein are injected intravenously and the migration of the dye through the blood stream and the interstitial spaces is observed under long wave ultraviolet light.

As a result of studies in artificially frostbitten animals (5), it was established that, for periods from 30 to 120 minutes following exposure to severe cold, no fluorescein appears in the exposed areas thus indicating a severe spasm of the arterioles. This condition is followed by a second stage during which *all* blood vessels reopen and fluorescein can be seen throughout the exposed areas. The diffusion of the dye into the surrounding tissues in this stage is many times greater than it is in the nonexposed skin due to increased capillary permeability; the picture of intense hyperfluorescence in the previously frozen areas is thus produced. This period is also characterized by marked swelling of the exposed region. Eight to 14 hours after exposure, a repeat fluorescein injection shows that now the exposed spots are nonfluorescent indicating a pregangrenous state. This nonfluorescence increases in the next hours until finally the entire locus is nonfluorescent and becomes gangrenous. Biopsy specimens taken at this time show that, in agreement with the findings of Green and Kreyberg, there is a clumping of red cells in the dilated smaller vessels. This clumping is probably due to loss of plasma through the highly permeable vascular wall. The red cells are stranded and silt the blood vessels, thus forming a sludge. They do not, however, represent *true* thrombi. The simple injection of saline enables one to wash out these erythrocytes as individual cells. Only after at least 72 hours does organization of these cells occur. This organization ultimately leads to infarctive gangrene. It is during the prethrombotic sludge phase that the therapeutic attack must be initiated to avoid thrombosis and ultimate infarctive gangrene, as promptly as possible following exposure and, ideally, before thawing is complete.

Animal experimentation substantiated the fact that the timely use of heparin prevented gangrene, whereas control untreated animals uniformly developed gangrene commensurate with the degree of frostbite.

It was now essential to apply these experiences to the human. The practical demonstration of the therapeutic value of heparinization in the prevention of gangrene was made possible by the study of artificial frostbite in human volunteers. These volunteers were recruited from patients who were being treated for subacute bacterial endocarditis by the combination of penicillin and heparin (6).

This investigation in human volunteers had a twofold purpose: first, to corroborate animal experiments and, second, to evolve a simple practical method for the heparin treatment of frostbite. The subcutaneous heparin prepar-

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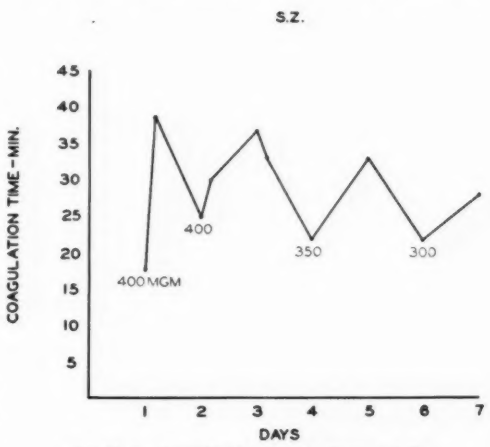
TABLE I.

HEPARIN—PITKIN MENSTRUUM FORMULAE

With vasoconstrictors	LP-0 mgm.	LP-8 mgm.	LP-9 mgm.	LP-12 mgm.
Crystalline sodium salt of heparin	100.0	200.0	100.0	150.0
Epinephrine hydrochloride	1.0	1.0	1.0	1.0
Ephedrine sulfate	25.0	25.0	25.0	25.0
Chlorbutanol	0.5	0.5	0.5	0.5
Eucupin dihydrochloride	1.0	1.0	1.0	1.0
Pitkin menstruum q.s. ad.	1.0c.c.	2.0c.c.	2.0c.c.	1.0c.c.
Without vasoconstrictors	LP-14 mgm.	LP-11 mgm.	LP-10 mgm.	LP-13 mgm.
Crystalline sodium salt of heparin	100.0	200.0	100.0	150.0
Chlorbutanol	0.5	0.5	0.5	0.5
Eucupin dihydrochloride	1.0	1.0	1.0	1.0
Pitkin menstruum q.s. ad.	1.0c.c.	2.0c.c.	2.0c.c.	1.0c.c.

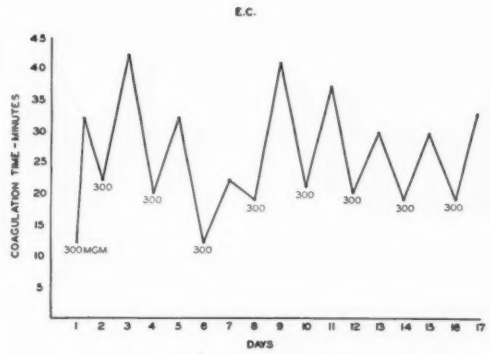


Graph 1. Coagulation time in Case 2, S.Z.

tion in the Pitkin menstruum (7, 9) seemed uniquely applicable in this connection. The intravenous administration of the aqueous commercial preparation of heparin would involve a more elaborate set-up than the simple intramuscular or subcutaneous injection of the drug in Pitkin's menstruum. This method of depositing heparin achieves a consistent, retarded, and equal release of the anticoagulant. The Pitkin menstruum which was designed to regulate the rate of release of water soluble drugs, is composed of gelatine, dextrose, glacial acetic acid, and water in definite proportions.

Various formulae (Table I) have been developed containing variable amounts of heparin in the Pitkin menstruum with or without vasoconstrictors. The vasoconstrictors have an additive prolonging effect. By combining the injection of various ampuls, one is able to employ greater or lesser amounts of heparin with or without vasoconstrictors.

The method of administration is as follows: the contents of the ampuls are liquefied in hot tap water, drawn up through a 2 to 2½ inch, 18 gauge needle, into a 5 or 10 cubic centimeter syringe and injected subcutaneously, preferably into the anterior or lateral aspect of the thigh. The pain and the discomfort is variable and transitory. The injections are given, as a rule, every day or every other day, and the average dose is 300 milligrams of heparin. Occasionally, 400 milligrams is required. The correct dosage is estimated by following the coagulogram as determined by the Lee-White modification of Howell's method. By this method the average control coagulogram is 9 to 15 minutes. Prolongation to 30 minutes to an hour is considered a satisfactory response. The response to the preparation is predictable in most instances as judged by observation of its clinical deportment in considerably over 1000 depositions administered in well over 200 patients suffering from subacute bacterial endocarditis or thromboembolic disease. The anticoagulant effect may be markedly depressed by the application of ice bags to the site of the deposit or may be accelerated by the local application of heat. Because of the urgency for obtaining prompt, adequate anticoagulant effects in the treatment of frostbite, a larger initial dosage such as 400 milligrams was employed at times in conjunction with local heat. In this manner, anticoagulant activity was observed within an hour.



Graph 2. Coagulation time in Case 3, E.C.

Fig. 1.

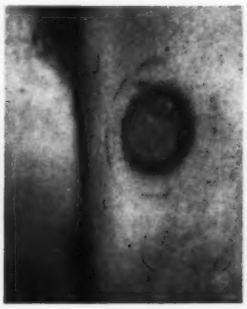


Fig. 2.

Fig. 3.

Fig. 4.

Fig. 5.

Fig. 6.

Fig. 7.

Fig. 8.

Fig. 9.

Fig. 10.

Fig. 1. S.F., male. Two days after exposure to a crucible filled with dry ice applied for 10 minutes to the upper arm.

Fig. 2. The same patient 4 days after the dry ice exposure.

Fig. 3. The same patient 17 days after the dry ice exposure.

Fig. 4. S.Z., male. Two days after exposure to a crucible filled with dry ice applied for 10 minutes to the upper arm. Heparinization started immediately after the exposure.

Fig. 5. The same patient 4 days after the exposure and after the start of heparin treatment.

Fig. 6. Same patient 17 days after the exposure and 11 days after termination of the heparin treatment.

Fig. 7. E.C., female. Two days after exposure to a crucible filled with dry ice applied for 30 minutes to the upper arm.

Fig. 8. Same patient 8 days subsequent to the initial exposure and 2 days following a second exposure under the same conditions but which was followed immediately by heparinization.

Fig. 9. Same patient 20 days after the first exposure and 14 days after the second exposure which was followed by heparinization.

Fig. 10. Same patient 27 days after the first exposure and 21 days after the second exposure followed by heparinization.

The practical demonstration of the therapeutic value of the method was made possible by our study of artificial frostbite in eight human volunteers. In one group the frostbite was accomplished by means of a porcelain crucible filled with dry ice and applied, without pressure, to the skin of the lateral aspect of the upper arm for 10 minutes. An area about 2 centimeters in diameter came in contact with the skin. By this method a temperature of approximately minus 22 degrees C. was achieved. Heparinization was started immediately following the exposure. One volunteer served as a control. The other group was subjected to local refrigeration in the same manner but for two exposures of 30 minutes each. The initial or control exposure was permitted to develop for 6 days before the second frostbite was induced, immediately following which, treatment with the subcutaneous heparin in the Pitkin menstruum was initiated. The 30 minute exposure with dry ice results in temperatures considerably below minus 22 degrees C., and is comparable, as to the degree of exposure, to the frostbite suffered by aviators in high altitude flying such as nose gunners after demolition of the plexiglass protection, or gunners attempting to unjam guns without glove protection.

The metamorphosis of the untreated lesions and the repair following heparin therapy are shown in the following illustrated cases.

CASE 1. S.F., male, aged 33 years, control case. The patient was suspected of having subacute bacterial endocarditis although no organisms had been recovered from the blood stream on repeated trial. He had been accepted for treatment with penicillin and heparin, which however, had not as yet been started. A 10 minute application of dry ice produced a frosted, depressed area 2.5 centimeters in diameter with surrounding raised erythematous zone 0.5 centimeters wide. The refrigerated area was frozen stiff. About 2 hours later the area of central depression was pink and elevated with a small zone of surrounding erythema. The following day the peripheral erythema about the frozen area had disappeared. The lesion was gray-brown with superficial vesiculation and had become completely anesthetic (Fig. 1). By the fourth day the central gangrenous area with surrounding hyperemic zone had progressed further (Fig. 2). The lesion on the 17th day appeared as a healing lesion with the exception of a small, central, necrotic, ulcerated, crusted area about 3/8 of an inch in diameter (Fig. 3).

CASE 2. S.Z., male, aged 35 years, suffering from subacute bacterial endocarditis due to a gram-negative, anaerobic coccus of the Veillonella group. He had several courses of penicillin-heparin therapy and was at the time in a post-therapeutic observational period. He was given a 10 minute exposure similar to that given S.F. following which he was immediately given 400 milligrams of heparin subcutaneously without vasoconstrictors (2 LP 11, Table I). The coagulation time rose promptly to almost 40 minutes from a control of 18 minutes (Graph 1). The following day another 400 milligrams was given despite an adequate coagulogram of about 25 minutes, in order to bridge the initial critical period with optimum anticoagulant responses. He was given another deposit of 350 milligrams (LP 11 plus LP 13) 48 hours later and 48 hours after that a final 300 milligrams (2 LP 13). The graph indicates consistent and satisfactory heparinization. After 24 hours the initial depressed area was raised, gray brown in color with a superimposed vesicle about 1 centimeter in diameter (Fig. 4). Four days after exposure there was marked hyperemia of the exposed area (Fig. 5). The entire lesion resolved without necrosis as shown by a comparable photograph taken on the 17th day following the exposure, where almost complete healing is indicated (Fig. 6—see control Fig. 3).

CASE 3. E.C., female, aged 21 years, suffering from subacute bacterial endocarditis due to Streptococcus viridans. She was given a control frostbite by exposure to dry ice for 30 minutes. Two days after this exposure, an enormous blister involving the entire lesion was at its height (Fig. 7). Six days after the control frostbite was produced, a similar 30 minute exposure was effected below the control area immediately following which 300 milligrams of heparin in the Pitkin menstruum without vasoconstrictors (2 LP 13) was deposited subcutaneously in the lateral aspect of the thigh. The coagulation time rose from a control of 12 minutes to 33 minutes (Graph 2) and dropped to 22 minutes the following day at which time an additional 300 milligrams (2 LP 13) was given with a prompt rise to 42 minutes. Thereafter, 300 milligrams (2 LP 13) was deposited every other day. Heparinization was consistent and adequate with the exception of the 6th day. However, it is more than likely that the effective therapeusis was accomplished within the span of the first 6 days.

Eight days after the control exposure the untreated lesion appeared as a large, ruptured bulla with an indurated base. Necrosis was also evident. Two days after exposure, the heparinized frostbite lesion was large, bullous, and without induration (Fig. 8). Necrosis of the control untreated area was still fairly extensive 20 days after exposure, but the heparinized lesion 14 days after exposure showed merely hyperemia and dilatation of the blood vessels without loss of tissue (Fig. 9). The complete necrosis of the untreated area is effectively portrayed 27 days after the control exposure. This

contrasts with the almost complete healing of the treated heparinized lesion 21 days after exposure (Fig. 10).

SUMMARY

1. The functional pathology of frostbite is discussed and the early heparinization of patients with such lesions is suggested.

2. Heparin in Pitkin's menstruum deposited subcutaneously or intramuscularly is a simple and satisfactory method of achieving effective anticoagulant responses.

3. Eight volunteers were exposed to small areas of frostbite by the use of dry ice. None of them developed any tissue loss when effectively treated with subcutaneous heparin while the control lesions showed central necrosis.

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MILITARY SURGERY—UNITED STATES ARMY—EUROPEAN THEATER OF OPERATIONS, 1944-1945

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MISSION OF UNITED STATES ARMY MEDICAL DEPARTMENT

THE Medical Department of the United States Army has a threefold mission—first, evacuation of the wounded, both from the battlefield, where their presence jeopardizes morale, and from the Army hospitals, where their care infringes upon the mobility and supply of combat forces. The second function is that of professional medical care. For this purpose an organization must be set up that brings the battle casualty and the medical officer together and provides the medical officer with those facilities necessary for such care. The third function is that of the restoration of injured men to combat. The number and percentage of wounded who can thus be returned to combat may, in a war of attrition, dictate success or failure. The medical departments of other armies may have other objectives—certainly, our inability to capture wounded Japanese in any number suggests that the medical department of the Japanese Army has a different mission.

ORGANIZATION OF ARMY MEDICAL DEPARTMENT, EUROPEAN THEATER OF OPERATION

To accomplish this threefold mission, there must be a carefully integrated organization, and some understanding of this is desirable if one is to appreciate the results which it has achieved. A primary consideration is the complete interdependence of administration and professional care, on which depends its effectiveness. The civilian doctor is prepared to expend every ounce of energy and all of his time on a single patient, knowing that others can be found to care for additional injured or sick people who might present themselves at the same time. This policy, when one is confronted with thousands and not individuals, must be forgotten in the greater good for the larger number. This change of outlook from the individual to the mass is the chief difficulty confronting the civilian doctor when he enters military service. Moreover, if the three functions of the Medical Department are to be fulfilled—evacuation, medical and surgical care, and restoration to combat fighting—attention must be focused more and more on those who can be returned to duty. By so doing, eventually a greater good for humanity will be achieved, for if large numbers of men can be restored to the fighting forces, war will end sooner and thus humanity suffer less. This need not result in neglect of the severely damaged soldiers.

The organization for medical care in the United States Army begins at the battle front and extends through to hospitals in our communications zone in a theater of war, from which the soldier may be returned to the combat forces, or through to hospitals for rehabilitation in the United States of America. Charts 1 and 2 present graphically the course of the casualty from front to rear. The care of the wounded soldier begins on the battlefield; there Company Aid men render first aid care. They control hemorrhage, dress the wounds, initiate sulfonamide chemotherapy, control pain with morphine, splint fractures and evacuate the wounded to the Battalion Aid Stations in the forward part of the combat division. The devotion and training of the medical soldier—of whom more than 2,000 have been killed in action in this theater—has been a major factor in the good results achieved by the medical department in this theater. At the Battalion Aid Post, where there is a medical officer in attendance, dressings are checked, splints readjusted, plasma is available if required, tetanus toxoid should be given, and the field medical record, if it has not been initiated by the Company Aid

Hunterian Lecture, Royal College of Surgeons of England, June 14, 1945

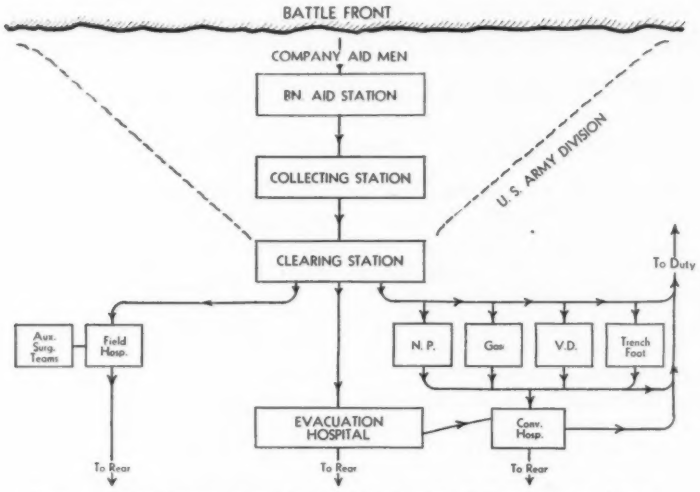

Chart 1. United States Army Medical Organization. I, Forward area (Army).

man, is properly filled out. Evacuation from the Battalion Aid Post may be by hand litter, or by jeeps with improvised litter racks, or even by ambulances. In the standard United States Army organization, such transport would be to a station at about the midpoint of the Division, known as a Collecting Station. At these points the dressings should be inspected and reinforced if necessary, but not taken down since each dressing adds further contamination. Here splints can be readjusted; warm food in the way of hot drinks is available; the field medical record is further completed and a check carried out as to the tetanus toxoid injection. From such collecting points, ambulances should carry the patients to the rearmost point in the Division, where the Clearing Station is located. Here begins sorting or triage, a function which continues throughout all hospital installations.

The Clearing Station has a limited number of beds, and lightly injured and nonseriously ill soldiers may be held there and from this point returned to duty without leaving the limits of the Division. It has been well established that the further down the line a soldier goes, the more difficult it is to return him to the combat forces. Because of this, and in order to increase the holding capacity in the divisional area, small tented units have been made available for special functions, such as the care of venereal disease and neuropsychiatric cases and, during the recent winter, the care of those with mild trench foot. The Clearing Station, having determined that such cases are simple or nonserious, and may remain at this level, makes such disposition. Its next sorting is to divide the battle casualties and more seriously ill into two groups; first, those who are seriously damaged and cannot travel far without immediate surgical assistance and, second, those who may travel further. The first group go to the platoon of a Field hospital. The Field hospital is a tented unit of 400 beds, capable of division into three platoons with 100 beds in each. It was not originally intended for this function, but was the unit best suited for its present use and has proved highly satisfactory. A Field hospital platoon can hold between 80 and 100 casualties. It is set up in juxtaposition to the Clearing Station, so that carrying from one to the other is by hand litter. The categories of those cared for in the Field hospital comprise those injured in the abdomen, the chest, those with serious damage to the face and neck, whose respiration is interfered with and who may need immediate tracheotomy and, finally, any other casualties whose condition is such that evacuation further would jeopar-

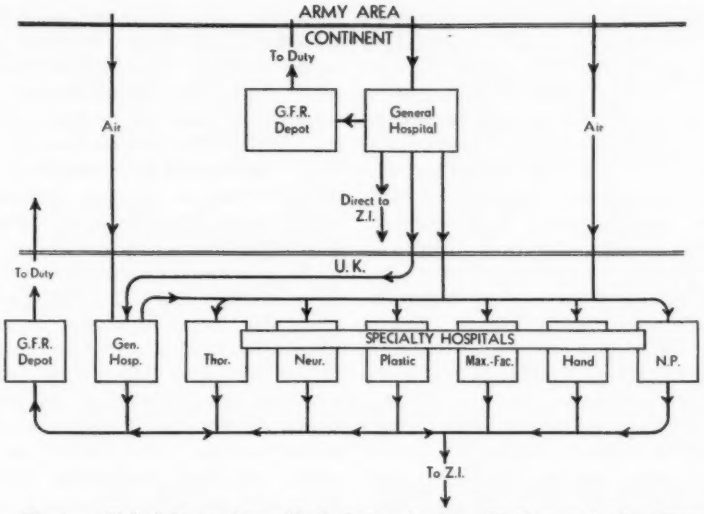

Chart 2. United States Army Medical Organization. II, Communications Zone (Continent and United Kingdom.)

dize their opportunity to survive. Such may be those with multiple, serious fractures. All other battle casualties by-pass the Field hospital and go further to the rear to an Evacuation hospital. This sorting at the Clearing Station is a function of greatest importance, and must be by experienced officers.

At the Clearing Station whole blood is available, and those who can travel following a transfusion of blood and/or plasma receive such treatment there. Also at this level treatment with penicillin is begun and from this point to the rear penicillin is available for regular parenteral injection. In the early part of the recent campaign, sulfonamide therapy, begun on the battlefield by the Company Aid man, was continued to the Evacuation hospital, and a majority of individuals for a few months received simultaneous treatment with the sulfonamides and penicillin. As time passed, and penicillin was in liberal supply, the continued medication with sulfonamides gradually diminished, until now it is practically reserved—other than the initial dose on the battlefield—for areas where penicillin is not available.

Each Army controls two special medical units—a Convalescent hospital and an Auxiliary Surgical Group. The Convalescent hospital has 3,000 beds and usually has a policy permitting the holding there of soldiers who may be returned to duty within 10 or 14 days. If sick and wounded require a longer period, they would not stop at the Convalescent hospital, but pass to hospitals in the Communications Zone. The Auxiliary Surgical Group is an assemblage of 61 surgical teams, the majority of which are headed by general surgeons, though there are attached special teams in orthopedic surgery, neurosurgery, thoracic surgery, maxillofacial surgery, and the treatment of shock. These surgical teams do the professional work in the Field hospitals, which are not staffed with expert surgeons, and also bolster up the Evacuation hospitals where there may be an insufficient number of surgeons for the load imposed. The professional abilities of these team surgeons have played a major role in the diminution of mortality rates. The rapidity with which younger surgeons improved their technique and acquired judgment is a great tribute to their fundamental training in the medical schools of the United States of America. The existence of such an organization permits the movement of surgical teams at any time to an overloaded hospital and effects a saving in highly trained professional personnel.

The organization for care in the Communications Zone (Chart 2) is built around the professional work in General hospitals. These are ordinarily 1,000 bed institutions, capable of expanding to 1,500 beds, but may be larger. Such General hospitals are frequently grouped together in what are called Hospital Centers, which greatly increases the flexibility of care and evacuation, and decreases the number of highly trained personnel required. Thus, if ten hospitals can be grouped together, a service can be established in selected hospitals for the care of special types of injury. These are generally divided into centers for thoracic surgery, neurosurgery, maxillofacial and plastic surgery, and for the care of those injured in the hand. Because of the local situation in this theater, we provided ourselves with hospitals of this type both on the Continent and in the United Kingdom. Early in the campaign, all of the centers for such specialist care were in the United Kingdom and in these special hospitals the greater percentage of such care was accomplished. This grouping of casualties under highly trained experts led not only to splendid care of the individual case but provided sufficient material to permit critical evaluation of methods of therapy which led to a steady improvement in our technical procedures. Finally, from hospitals in the United Kingdom, or on the Continent, evacuation both by air and sea had to be provided for the patients who could not be returned to duty and who should be returned to the United States of America.

This entire system of hospitalization is flexible, for it must vary with the military situation, since the tactical action and the numbers of casualties resulting from such activity dictate the theater policy for evacuation. Almost to the end of the campaign this theater functioned under a theater policy of 120 days, which meant that any sick or wounded soldier who could be returned to duty within 120 days could be held in the hospitals of the European Theater of Operations. Because of the difficulty of evacuating soldiers to and from the United Kingdom, an additional policy was established relating to which cases should be hospitalized in the United Kingdom and which should be held in Continental hospitals. As a rule, long term cases went to the United Kingdom, and those who could be shortly returned to duty remained in Continental hospitals; but when casualties were reaching between 40,000 and 50,000 per month, and when the Continental hospitals could not hold all those who would be returnable to duty in 60 days, or even in 30 days, modification of the policy came into being and many who were returnable to duty in 60 days or even less had to be evacuated to the United Kingdom and then brought back to the Continent when ready for duty. Similarly, it was inevitable that in the rush of work (60,000 patients were moved by air in May), individual casualties who perhaps could never have been returnable to duty, even in 120 days, were mistakenly routed and had to be held in our Continental units, but these incidences must be looked upon as unusual.

All this emphasizes that only the perfect interdigitation of administrative and professional personnel can lead to a happy solution when thousands of wounded men are handled daily. Professional personnel must be informed where the load is to be borne, how long casualties can remain in one hospital, and what methods of evacuation are to be used if proper care is to be given. And personalities must be forgotten. In spite of difficulties, the professional group always attempted to carry out the policies set by the chief surgeon, both those which placed a time limit on professional care and that which demanded of us that the American soldier be given the best care possible under the conditions imposed by the military situation. Administration must set evacuation and hospitalization policies, but these policies and the burden they impose are borne by others. Good results will accrue only when both are completely informed of the labor and responsibility of the other. Directives are no substitute for good briefing, whether the goal be tactical or medical.

Sorting at the Clearing Station has already been dealt with. Further sorting is carried out in the Field hospital. Here with each admission an appraisal of the patient's condition will dictate what kind of resuscitation is necessary; whether the presence of a tourniquet demands immediate priority for the oper-

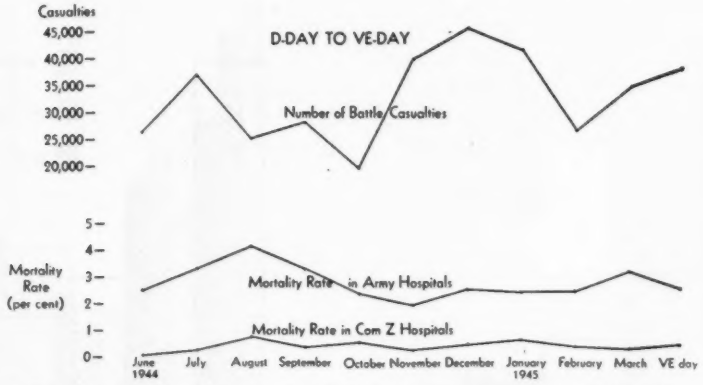

Chart 3. Battle casualties, Medical Department, European Theater of Operations, excluding K.I.A. Total battle casualties, 372,556; mortality rate, 3.9 per cent.

ating room, or whether the missile's course and lodgment requires an x-ray examination before the surgical ordeal.

Again, after the surgical intervention, further evaluation and sorting distinguishes between those who can stay and those able to be evacuated. The same kind of sorting, evaluation, and triage must go on in every hospital. Let us consider the importance of proper sorting at the first General hospital the casualty enters after leaving Army installations. Here a dual function confronts the hospital—the wounded who have slipped through the Army hospitals without primary care must be given that care, and those who have received primary care and those now given it in this hospital must be routed after sorting, according to the evacuation policy at that time. Again, consider the less busy General hospital in the rearmost area. Casualties may reach this hospital on the third or fifth day. The question immediately arises—which wounds can be sutured and which must be left open? All military surgeons must recognize that this constant evaluation and sorting into special categories for evacuation or professional care is a major function for the medical officer.

STATISTICAL DATA ON MORTALITY RATES AND DISPOSITION

Certain statistical data are presented at this point, not to emphasize the immensity of the task now just completed, but to demonstrate that the results achieved in this war differ sufficiently from those in World War I to demand an estimation of the factors that have brought about these improvements. Also, lessons may be drawn that will benefit our casualties resulting from the growing conflict in the Pacific.

Chart 3 summarizes the United States Armies', European Theater of Operations, total wounded in action casualties from D-day through VE-day, and presents the overall mortality rate of these casualties in medical installations. This mortality rate of 3.9 per cent in 372,556 battle casualties is approximately one-half of the rate in the first world war. Of the 3.9 per cent mortality, about 0.5 per cent die within the medical elements of the combat division (Battalion Aid Post, Collection Station or Clearing Station), 2.7 per cent die in Army hospitals (Evacuation and Field hospitals) and less than 1 per cent in General and Station hospitals in the rear area.

The next three charts present comparative statistics for anatomical woundings. Chart 4 compares the regional distribution of the wounds in the casualties reaching medical units alive, in the United States Civil War, World War I, and World War II. The increased percentage of wounds of the thorax and abdomen in this war as compared to World War I represents in part a higher survival rate, possibly through better care on the battlefield and better evacuation. Some of

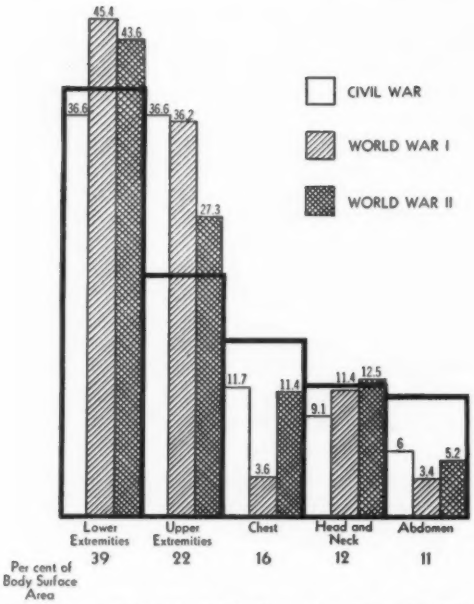

Chart 4. Regional distribution of wounds in WIA (wounded in action) casualties during 3 wars.

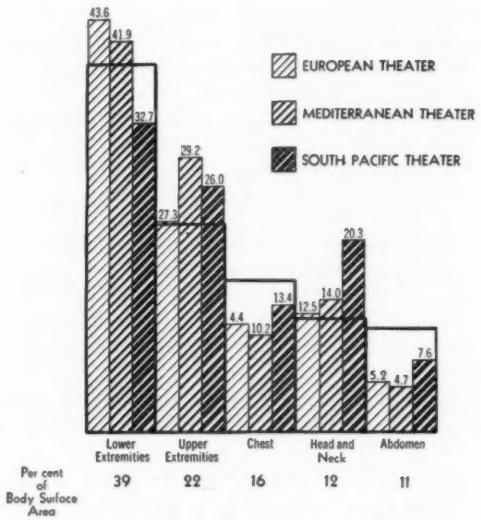

Chart 5. Regional distribution of wounds in WIA (wounded in action) casualties in different theaters of World War II.

the percentage variation is doubtless attributable to a shift in the standards for body surface and some due to the lethal effect of changing weapons.

Chart 5 presents variations occurring in different theaters in this war. The significant increase in wounding of the head, face and neck, from 12.5 per cent to 20.3 per cent in the South Pacific theater bespeaks fighting at close range, as must occur in jungle combat. This information should be of great value to medical units now being redeployed to that theater, for such units should be plentifully equipped with personnel and material for this added burden.

Chart 6 compares United States Ground Force and United States Air Force statistics. Again, the high percentage of face and head wounds amongst Air Force casualties is due to tactical reasons. Also, the reduction in the percentages for thoracic and abdominal injury reflects credit on body armor as used by the United States Army Air Force.

Chart 7 is a study of injury by missiles in the different theaters of war. The outstanding variation is the great increase in small arms injury in the Pacific fighting on certain islands (Leyte and Saipan), again a tactical reflection, for jungle fighting must obviously lead to the greater use of small arms. Again, these data can be of great value in the professional education of units about to be redeployed to new theaters.

Finally, the third mission of the Medical Department, to return the wounded to combat duty, is reflected in Chart 8. This shows the numbers of hospital patients returned to duty through the Ground Force Reinforcement Command depots. It is seen that battle casualties return to full duty in a far higher percentage than do those classified as nonbattle injury and disease. Our ability to return to full duty from hospitals 80 per cent of battle casualties respresents our competence in accomplishing this mission. Obviously, the neuropsychiatric casualties do not return to combat in any great number (8.5%). It is noteworthy that of all groups returned from hospitals to the Ground Force Reinforcement Command, less than 1 per cent of them have to be sent back to hospitals for further treatment.

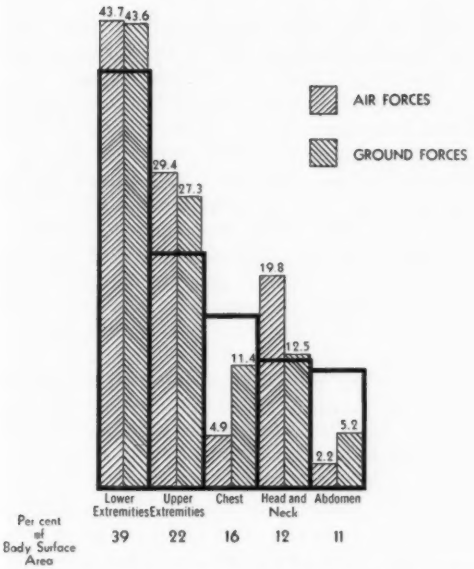

Chart 6. Regional distribution of wounds in WIA (wounded in action) casualties sustained by the Air and Ground Forces during World War II.

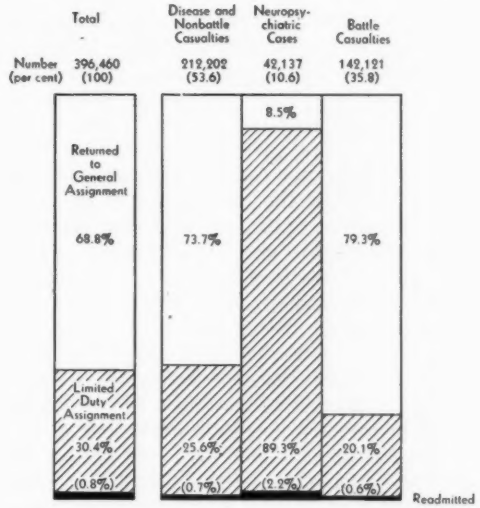

Chart 8. Disposition of 396,460 hospital cases sent to duty through the Ground Forces Replacement Command. European Theater of Operations, June 23, 1944 to May 4, 1945.

PROFESSIONAL CARE

The professional aspects of the care of the sick and wounded in the European Theater of Operations have been carefully laid down in a *Manual of Therapy* and in circular letters from the Office of the Chief Surgeon. These directives were set up after the most careful study of all data which the Professional Services Division in the Office of the Chief Surgeon could assemble. Much of it came from data acquired by our colleagues in the Mediterranean Theater of War; for a great deal of it we are indebted to our British colleagues, either data collected by them from the many British theaters of war, or experiences of individual officers themselves. These directives instruct our medical officers in what should be done to the wounded man, all the way from the battlefield to the rearmost hospital. Details are given pertaining to the use of blood and plasma for resuscitation; the proper dosage of the sulfonamides and penicillin; the toilette or débridement of a wound; the optimum methods of caring for fractures, both during transportation and during the period of healing in General hospitals. Each specialist has contributed to his field and, above all, the officers of the Medical Corps, scattered throughout the entire theater, have been willing to assimilate these standardized methods and have greatly improved the original directives by suggestions and additions as experience hardened our opinion or showed flaws and defects in the original methods outlined.

This willingness to accept standardization, the thirst for education in military surgery, and the ability to improve on original standards, has characterized our professional colleagues from the very beginning.

The one item in professional care which distinguishes care in this war from care in World War I, as well as the single factor most

CHART 7. PERCENTAGE OF WOUNDED HIT BY MAJOR CAUSATIVE AGENTS

Source of data	High explosive shell fragments	Bullets	Other
First Army, June–July, 1944	67.3	29.0	3.7
Fifth Army, January–December, 1944	78.1	18.1	3.8
XXIV Corps, Leyte	42.6	52.7	4.7
27th Division, Saipan	50.7	46.7	2.6
Bougainville	70.2	27.4	2.4

directly contributing to the improvement of morbidity and mortality statistics, is the resuscitation of the wounded man. This transcends in importance any single method of therapy, such as our ability to procure and deliver blood and plasma to casualties, for it betokens that the American surgeon has at last appreciated the importance of the complete evaluation of his patients before therapy. He has learned to care for the whole of man and not for any fragment or any particular wound. This, in turn, has led to proper resuscitation and the better care of shock. Accretions to our knowledge concerning shock have come in steadily as experience has been acquired. Dependable studies of blood volume made in forward hospitals indicate that soldiers seriously damaged have averaged a loss of at least one-third of their total blood volume, and investigators have tried to set simple standards for recognizing this deficiency. Majors Emerson and Ebert have stated that a blood pressure below 85 systolic usually betokens a loss of over one-third of the total blood volume. Professor McMichael of the British Post Graduate Medical School has stated that in the male thigh an increase in diameter of some 2 centimeters which, to the cursory glance, would not seem great, may mean that 1500 cubic centimeters of blood are outside of the capillary bed and actually beyond the vascular tree.

This is a matter of great importance. Surgeons are apt to think that only when there is visible blood loss is the condition of the patient jeopardized, but it can be seen that 3,000 cubic centimeters of blood may be lost from the circulation when there are wounds in both thighs, without more than a few drops leaving the body. It is this overall appreciation of diminution in the amount of circulating blood, and this overall desire to look at the whole man, and not the wound alone, that has led to our greatest advance in this war. From May 22, 1944, to May 31, 1945, 385,231 pints of blood have actually been used in medical installations in the European Theater of Operations. Of this, 194,712 pints were flown directly from the United States of America. This blood has been available as far forward as the Clearing Stations in Combat Divisions. It has been used largely in the Field and Evacuation hospitals in the forward area at the time of primary surgical therapy, and has been used in great quantities, up to 6 or 7 liters in a single individual in one day. This widespread use of blood, through its easy availability, has brought in its train inevitable reactions, as well as great benefit. The best figures available at this time show that about 4.8 per cent of transfusions are followed by some kind of reaction: allergic reactions, 0.9 per cent; pyrogenic reactions, 3.7 per cent; hemolytic reactions, 0.1 per cent. The reactions vary in different types of institutions, and vary as to whether the transfusion is given early or late. As a rule, primary transfusions have brought little reaction. Later transfusions, given in General hospitals, have often found the patient sensitized by the earlier transfusions. Pyrogenic reactions have increased where hospitals insisted upon cleaning their own glassware and not using sets furnished to them already clean and sterile. As time has gone on, reactions have diminished, probably because of better technique, better refrigeration of the blood, and through our ability always to furnish giving sets properly set up and sterilized at some central point. A particularly valuable study of these reactions following transfusion has revealed that the transfusion of large amounts of group O blood (the universal donor) and even of pooled plasma, may result in serious hemolytic disease. The implication is strong that, whenever feasible, strictly compatible blood of the same group as the patient should be used; that where large amounts of group O blood must be used, only blood of a low titer should be administered. Such information as this, and other studies now in process, will doubtless have some influence on the future set-up of blood banks in civilian life.

Chart 9 depicts the use of the varying anesthetic agents in over 360,000 cases. It is of interest to see, as would be expected, that the inhalation anesthetics are largely used in the forward hospitals for nontransportable casualties, comprising almost 45 per cent of all anesthetics in Field hospitals. This is because a high percentage of the wounded there are injured in the thorax and must have endotra-

CHART 9.—ANESTHETICS ACCORDING TO METHOD USED JUNE 1944, THROUGH FEBRUARY 28, 1945, EUROPEAN THEATER OF OPERATIONS

Hospitals	General %	Station %	Evacuation %	Field %	Total	Total %
1. Inhalation	6.1	3.3	12.8	44.7	31706	8.7
2. Field blocks	26.4	38.0	26.5	21.2	101268	27.7
3. Miscellaneous regional	1.9	2.8	4.7	2.3	10143	2.8
4. Spinal	10.2	13.3	2.6	4.6	31028	3.5
5. Sympathetic	1.6	1.1	1.1	.3	4980	1.3
6. Intravenous only	36.3	29.2	44.2	20.1	134205	36.8
7. Intravenous combined	17.5	12.7	8.1	6.8	51105	14.0
8. TOTAL	210409 48416	93291	12428		364409	
9. Endotracheal	2.3	1.1	3.7	28.5	12332	3.4

cheal anesthesia. Another comment is suggested by the increasing use of regional or local anesthesia. It would seem that regional anesthesia is not, *per se*, the anesthetic of choice when a wound must be widely débrided and much tissue excised. Regional anesthetics tend to limit the surgeon. They may thus result in inadequate débridement of the wound and, unless there be other contradictory evidence, it would seem wiser to render the patient insensitive as a whole for complete toilette of the wound. The high percentage of procedures carried out under intravenous (pentothal) anesthesia represents the usefulness and desirability of this method.

The débridement of the wound is the most important surgical task. It is of major importance for the end-result, both as to life and as to function. If properly done, it should obviate serious infection. It may preserve a limb from amputation and, if blood supply is intact and major nerves undamaged, will leave good function. In the first place, the surgeon should always attempt to visualize the position of the patient at the time of the injury. This has been difficult to teach. Thus, a wound over the heart does not necessarily mean that the solider is wounded in the heart, for if the soldier was lying down, the missile may have traveled a great distance under the skin and have done almost no damage, and emerge close to the hip joint. Similarly, if the arm is flexed when hit but operated upon in the extended position, the tract of the missile cannot be properly débrided unless the arm is again placed in the flexed position, as it was when the missile traveled across the bellies of the muscles. We have watched a young surgeon attempting to find a missile in the inner condyle of a knee—a missile which entered when the knee was in the flexed position; but the surgeon was operating upon his patient with the knee extended and thus failed for some time to locate the course of the missile and therefore unnecessarily damaged an important joint surface.

Another matter which must concern all military surgeons is what can be spoken of as wound ballistics, or the application of physics to wounds. As early as 1914 it was shown that there was a definite relationship between the extent and severity of a wound and the kinetic energy (*i.e.* mass or size times velocity) of the missile producing the wound. The criterion put forward originally was that 58 foot pounds of energy were required to produce a casualty. However, this original criterion was based on observations pertaining to bullets weighing an ounce or more. During the present war, investigations have been carried out on the wounding power of very small, high velocity fragments, and it has been proposed that a new casualty criterion be set up on the momentary cavity which these missiles produce in tissues or experimental media. Although surprise has often been expressed at the large cavitation produced in soft media when a small missile passes through it, it can be shown that this cavitation is to be expected, and that the same physical principles apply to its formation in soft and hard media ranging from soft gelatin to hard steel.

When a missile passes through a medium, that portion of the medium which lies just

ahead of the missile must move aside with a velocity somewhat less than, but comparable to, that of the missile that has imparted some of its energy to the tissue. The extent of radial movement or cavitation of the tissue in the path of the missile depends upon the strength of the "restoring" force of the medium. Thus, the "restoring" force of steel, or the tendency of the elasticity of the steel medium to reverse its direction of movement, is great, and the distance it moves radially along the path of a missile is minimal, doubtless in most cases a small fraction of a millimeter. In contrast with steel, whose "restoring" force is approximately 100,000 times greater than 20 per cent gelatin (which is comparable in density to human skeletal muscle), in the latter a momentary cavitation is produced along the path of a missile passing through. Associated with the cavitation produced by a missile passing through a medium at a high velocity, there is considerable damage to the medium at considerable distance from the missile tract. In instances where the medium is living tissue, nerves, vessels, and even bones may be severed or broken when a high velocity missile passes in the proximity of, but not necessarily through, such a structure. An appreciation of these facts is essential to proper débridement of a wound, and explains the necessity for wide débridement.

Let us now consider the actual carrying out of the débridement of a wound. In the first place, proper preparation of the skin over a wide area must be performed. Soap and water is satisfactory, but any good detergent, such as ether, gasoline or zephyran, may be used. This may be followed by alcohol or, if the surgeon is wedded to dyes, merthiolate. Next, the incision must be in the long axis of the body, and sufficiently long to expose well every recess of the wound. A minimum of skin should be removed, partly because skin is essential to proper early closure of the wound, but also because skin itself is not alone the site of widespread infection. Only a minimum of 2 or 3 millimeters at the contacted edge of the tract need be cut away. Fascial planes below this should be widely opened and, where there is tough fascia, as in the thigh, it is better to cut this transversely as well as longitudinally. When one is concerned with the next layer, muscle, the major problem arises in the proper débridement of a wound. All devitalized and dead muscle should be excised. Hesitation to do this often results in disaster. Live muscle is determined by its ability to contract and by its color. If the wound is filled with salt solution after hemostasis, dead muscle loses its color more rapidly than living muscle, and all frayed fragments can be more easily detected. Once the surgeon is satisfied with the muscle excision, which must, in perforating wounds, involve both aspects of a limb, he must carefully determine the condition of the nerves and blood vessels. These are the most important elements in an extremity. Blood vessels should never be ligated when the opening can be closed by a suture and, if ligation seems essential, some form of tube, if available, should be inserted. The idea is to permit some blood to enter the extremity for at least 3 or 4 days, until the collaterals have been given time to dilate and take over normal blood flow. In our opinion, heparinization of casualties, when there is the possibility of internal concealed hemorrhage, or where there are multiple wounds, carries too high a risk of secondary hemorrhage, and should be condemned.

Next, one must be concerned with the nerves. If these are divided it seems wiser to approximate them loosely with a single loop suture of metallic substance, such as tantalum, in order that one may find the severed nerve at the time the nerve suture should be carried out, and to prevent their retraction to the deeper recesses of the wound. Suture of the nerve at this time in a contaminated area is not good therapy and, in fact, it has been shown that the axis sheath is much more likely to accept and guide new processes into the sheath after an interval of 3 to 6 weeks.

Bony fragments, unless they are absolutely loose and unattached to the periosteum, should not be removed, for now that the danger of infection has been mitigated by the advent of the sulfonamides and penicillin, we must leave every piece of viable bone in the wound in order that nature may reconstruct the damaged part herself. No bone graft can ever hope to equal natural healing. All soft

tissue wounds not leading to the cavities within the skull, the thorax and the abdomen, must be left open; in spite of modern chemotherapy, infection remains a major risk, which is vastly increased by primary closure of the wound.

Finally, the dressing. As experience has accumulated, it is obvious that much damage is done by packing wounds open. Ideally, in very deep wounds a small slip of rubber tissue should suffice for the escape of tissue juices, or a single piece of vaselinized gauze might be left in such wounds. Next, the wound must be properly bandaged. The advent of adhesive plaster has lost to the surgeon much of his art as a dresser, but the ideal dressing was well described by Sampson Gamgee almost 100 years ago; it should cover the wound completely and extend well beyond the wound to keep out further contamination. The dressing should contain enough substance so that when the bandage is applied it will be elastic and give gentle compression and comfort to the part. In turn, if the part is elevated, swelling is diminished, circulation is improved, and pain is minimized as the sensitive tactile end organs are no longer stimulated by pressure. In the greater wounds it is wise to add further means of immobilization. This may be only a splint, or better, a light plaster shell. The value of this immobilization of recently damaged tissue was perhaps overemphasized by the Spanish school, which felt that a limb should remain in plaster of paris until healing of the bone took place. Such prolonged immobilization led to a neglect of proper alignment of bone, though it did possibly assist, in the days before the sulfonamides and penicillin, in decreasing the spread of infection. This débridement of the wound is a major element in happy results. Chemotherapy has, indeed, revolutionized modern military surgery and opened up immense possibilities in the earlier and more complete restoration of function. But chemotherapy cannot effect sterilization of dead and devitalized tissues; surgery alone can be useful in such circumstances.

THE SURGICAL SPECIALTIES

Great advances have come during this war in each specialty. There are differences of opinion as to whether the specialist has a place in the forward zone, but the answer depends upon the definition of specialization. All surgeons, whether they be in a narrow specialty or a large one, should have first a broad general training in surgery. If this is the training of the specialist then he may be immensely valuable in the forward area.

Thoracic surgery has already laid down certain incontrovertible dicta for military surgery. First, conservatism in the forward area; only sucking wounds of the chest and pressure pneumothoraces, and the greater wounds, must be dealt with forward; the majority of thoracic wounds, except for the great necessity of keeping the pleural space emptied of blood, do better with a period of delay, and the more elaborate procedures, when they seem necessary, carried out in specialized hospitals in the rear area. The advent of chemotherapy has resulted generally in a decrease of serious infection in this field for work. A special word must be said for decortication of the lung, a procedure which has proved satisfactory up to the third, and even later than the fifth, week following injury, and also even when a very considerable amount of infection is present. The removal of a clotted hemothorax and decortication bears some relation to the removal of a subdural hematoma and, indeed, it may be that the increasing size of clotted hemothoraces bears a similar relation to the increased osmotic action of broken down hemoglobin, as it does in intradural hematoma.

The field for neurological surgery has made great advances. In our Army, those operated upon in the forward area are largely those actively bleeding, threatened with increasing intracranial pressure or with very large retained missiles. It has been observed that less serious intracranial damage withstands transport very well and that, in patients properly treated with penicillin, the advent of serious infection is no greater when such patients must wait 3 to 4 days before reaching a hospital for specialized care in the rear area. In the field of peripheral nerve surgery, equally important advances have been made. Our surgeons have made every attempt to close wounds as early as possible, and, in the large percentage with nerve damage, have sutured

these nerves at the optimum time in a clean field before returning such patients to the Zone of the Interior. Lately, our specialists have come to the opinion that when there exists injury both to bone and nerve, the definitive treatment of the fracture may even be temporarily postponed, on the basis that a flail limb is less useful than a crooked one. Thus, more and more early nerve suture has become the standard policy.

There has been no recent radical change in abdominal surgery. In principle, all small bowel injuries should be closed when possible, and when the blood supply is adequate. All large bowel injuries should be exteriorized by the simplest method available. These colostomies, in turn, should be closed as soon as possible in the General hospitals in the rear zone. Injuries below the rectosigmoid, which cannot be exteriorized, must be closed and a complete diversion of the fecal stream carried out proximally to the sutured area.

The combined thoracic and abdominal wounds constitute the greatest surgical problem. First, the surgeon must be sure that every wound of the shoulder or back, and every wound in the region of the thigh and buttocks, does not enter both cavities. The patient must have very adequate resuscitation and special attention must be given to his anesthesia. Finally, confronted with dual lesions, the surgeon must determine whether both can be done at the same sitting. If they cannot, the abdominal procedure must take precedence, just as it must take precedence when a neurological and abdominal wound occur in the same soldier. As has been pointed out earlier, most of the thoracic wounds can be temporized with. Such combined procedures often consume 2 or 3 hours, and strain the ingenuity and technical ability of the surgeon. It is to the great credit of the men working in our Auxiliary Surgical Groups that the mortality rates in this field remain as they are —between 30 and 35 per cent.

Special mention should be made of maxillofacial damage, particularly to instruct the military surgeons to save all skin and bone, and in the forward area to see that an open airway exists, even if a tracheotomy is forced upon the patient. The first step in the more elaborate reparative procedures can then be carried out in the General hospitals in the Communications Zone, before evacuation to the Zone of the Interior for the final, usually multiple, reconstructive procedures.

The treatment of the wounded hand deserves special consideration. This is, next to the brain, the most important fragment of the body for the ordinary citizen. It allows him to support himself and his family; to educate his children, and to live as others do. To fail in one's ability to support oneself brings about a mental attitude incompatible with good citizenship or as a useful member of a family. In considering the hand, one must remember it has a liberal blood supply and, like the face, stands primary closure under many conditions. We have permitted our forward surgeons to close a considerable number of such wounds of the hand, on the basis that if the skin can be closed, the fractures do quite well and their position can be remedied later. Special directives have been issued to cover this point, urging minimal removal of skin and bone, and stating that such primary closure of a wound can be permitted only if the patient can be held in the forward area for a period of at least 5 days, to observe whether serious infections will ensue. It is our impression at this time that this policy has saved many hands for a useful future.

A word should be written concerning orthopedic surgeons. Their ideas and their work touch upon every field. Many of the advances made in narrow specialties have come from their great labors and great experience. Their labors with plaster casts in the forward area and their skeletal-traction-suspension care in the General hospitals has been an Herculean task, yielding splendid results.

DELAYED WOUND CLOSURE

A fundamental feature of the surgical care of a wound is not to close it in the forward area, with certain exceptions, which have been mentioned. At the same time, in order to carry out one of the primary missions of the Medical Department—the early restoration to duty of the wounded—the wound must be closed at the earliest safe moment. Closure may be by suture, by graft or by a plastic

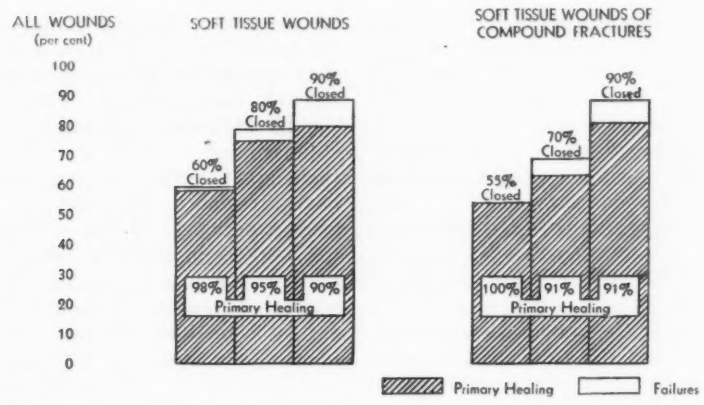

Chart 10. Increased "salvage" with great proportion of secondary closures attempted.*

procedure. Such a closure should be spoken of as "delayed." It is not a secondarily closed wound because it was never closed before. It is not delayed primary closure, because there has been no primary closure. We have had a large experience in this field. All our hospitals are instructed to close wounds at any time after the third or fourth day. The optimum time is certainly before 10 days, when granulation tissue and cicatrization have already begun to defeat any attempt to draw together the lips of the wound without a secondary cutting operation. It may be stated that around 75 per cent of all wounds are solidly healed 2 weeks or less after the delayed closure, and that at 3 weeks 90 per cent are solidly healed. Variations in these percentages will occur with individual hospitals. The most difficult task in this field has been to persuade our surgeons to attempt to close *all* wounds. Some surgeons report statistics where 95 per cent of their wounds thus closed healed *per primam*, but some of these surgeons do not attempt to close *all* wounds, and the figures for the attempted closure of all wounds, which represent the salvage for the Army, are the only ones of importance. Chart 10 reveals interesting data in this special field, collected from several different hospitals. When 98 per cent of soft tissue wounds healed *per primam*, only 60 per cent of all wounds were closed; when 90 per cent healed *per primam*, 90 per cent of all wounds were closed. In the latter hospital, though the healing rate was not so high, the ultimate salvage for restoration to duty was 20 per cent greater.

*Based on representative data from various General Hospitals.

In the closure of wounds of compound fractures, it is again evident that attempts to close wounds should be more universal; even if a lower percentage of wounds heal *per primam*, the salvage for future duty is greatly increased when this is practiced.

REASONS FOR IMPROVED STATISTICS

It would be impossible, at this time, to evaluate and put in proper perspective the reasons why the mortality rates in the United States Army in World War II are one-half as great as those in World War I, but there is every reason to believe that the following have each played a rôle:

1. *Resuscitation.* The proper treatment of the patient in shock, chiefly by the use of plasma and blood.
2. *Better first aid* by the Company Aid man on the battlefield.
3. *Penicillin and the sulfonamides,* which have vastly reduced the horror of infection.
4. *Improved methods of transport and evacuation,* which allow earlier meeting of surgeon and casualty, and more comfortable travel.
5. *Good general physical condition of the soldier.* This may be partly diet, or it may relate to the physical training to which he has been subjected before battle.

6. *Standardization of therapy* and the great medical and surgical educational programs emanating from the Office of the Chief Surgeon, European Theater of Operations. This did not exist in World War I.

7. *Better surgery*, through better anesthesia, better development of specialists and better training of the young surgeon in the Army.

The surgical technique has been put last to give full credit to obvious new advances that did not exist in World War I, and because no amount of good surgery could play such a major rôle in freeing the wounded from terrible infection. However, the great debt of every wounded soldier to his surgeon remains a hard fact.

TRIBUTE TO THE UNITED STATES CIVILIAN DOCTORS

In conclusion, it is fitting to pay a tribute to the civilian doctors of the United States. Of the 16,055 Medical Corps officers in the European Theater of Operations, over 97 per cent are civilian doctors who have been but recently commissioned. These civilian doctors have shown a willingness to conform to a standardized method of therapy that does them great credit. At the same time, they have revealed an immense capacity to learn from experience, and it is suggestions from the workers in the field, in all installations, both in the forward and in the rear areas, which have permitted us to improve consistently the methods of therapy originally outlined. Their ability to withstand great physical hardship, to subordinate themselves for the good of the Army, their ability to learn in the face of the conditions which have been imposed upon them in the forward areas, all show how very real are the personal attributes of these doctors.

THE ORIGIN, FREQUENCY, AND SIGNIFICANCE OF MICROSCOPIC CALCULI IN THE KIDNEY

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ALTHOUGH considerable interest has been focused on the pathology of the renal pyramid by the studies of Randall and other workers, we have been unable to find any published material quoting the exact frequency of microscopic calculi in the pyramids of the kidneys or an adequate description of their origin, morphologic characteristics, or possible significance. Most of the significant work has been done on the *macroscopic* patches or plaques appearing on the surface epithelium of the pyramid which points into the cavity of the renal pelvis.

We shall therefore define a microscopic calculus as a deposit of calcareous material appearing in the substance of the kidney, of a size sufficient to be seen easily under the ordinary low-power microscopic lens and measuring at least five to six times the size of the tubular cells.

For the original purposes of this study, unselected diseased kidneys removed surgically at the Mayo Clinic provided a basis for the conclusions. Kidneys which had been removed because of tuberculosis, pyelonephritis, hydronephrosis, or stones were studied. As the work progressed, it became evident from the findings that grossly normal kidneys removed at necropsy should be included. Accordingly, such a group was secured and studied in the same manner.

Careful histologic search was made for microscopic calculi in each pyramid, after the pyramid was cut, sectioned, stained with hematoxylin and eosin, and mounted. Calcareous deposits were sought on the basis of the foregoing definition. When a calculus was found, careful scrutiny as to the possible histogenesis was carried out. If the particular pyramid in one kidney did not show a plaque, further sections from other pyramids of this same kidney were studied in an effort to find such a lesion. This procedure was continued until the calculi were found in each kidney or their absence was shown beyond a reasonable doubt.

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Abridgment of thesis submitted by Dr. Anderson to the Faculty of the Graduate School of the University of Minnesota, in partial fulfillment of the requirements for the degree of M.S. in Surgery.

Randall noted the microscopic plaques and wrote, "The vast majority of papillary calcium salt deposits have been found to be intrapapillary and innocent of further pathologic change."

Vermooten made histologic preparations of the papillae from 103 kidneys which showed the grossly visible plaques on the surface epithelium of the pyramid. He noted the deposition of calcium in the collagen fibrils of the renal papillae in many of the sections but he did not state the exact frequency of this finding.

In 1862, Henle recognized deposition of calcium salt in the renal substance. He termed these deposits "calcium infarcts" and pictured the lesion as a complete filling of the tubules with chalk.

In 1904, Beer made a macroscopic and microscopic study of 100 kidneys removed at necropsy and concluded that deposits of lime in the kidney were a very common pathologic condition. He stated that lime is found in the tubular epithelium as fine granules. He found the deposits only in the parts of the kidney which he felt were diseased. He spoke of the lime being deposited in fine granules throughout the parenchyma of the kidney. He found calcium deposits in 53 per cent of his 100 cases but never among persons less than 24 years of age.

In 1933, Huggins studied surgically removed kidneys, all of which had come to operation because of massive stones. He described deposits of calcium beneath the epithelium of the collecting tubules.

W. Anderson reported on a study of tiny, single or multiple deposits of calcium salts in

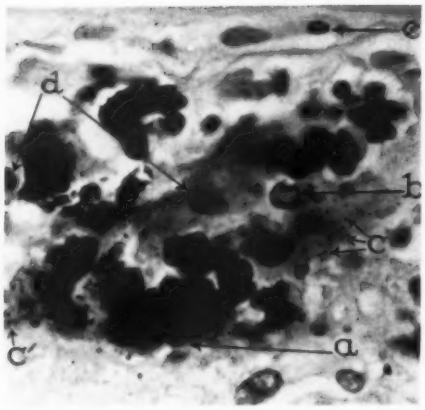

Fig. 1. Section of pyramid from a pyelonephritic kidney. *a* represents a small coalescing plaque of the type considered as minimal evidence of positive calcareous deposition; *b* is a phagocytic cell with a tiny bit of ingested calcareous material; *c* and *c'* are interpreted as bits or "flecks" of calcareous material which may subsequently be absorbed by a phagocytic cell; *d* represents "droplets" about which can still be seen a remnant of the phagocytic cell membrane; *e* represents "droplets" which have lost all cell membrane but which have *not* yet coalesced into a microscopic calculus. ×620.

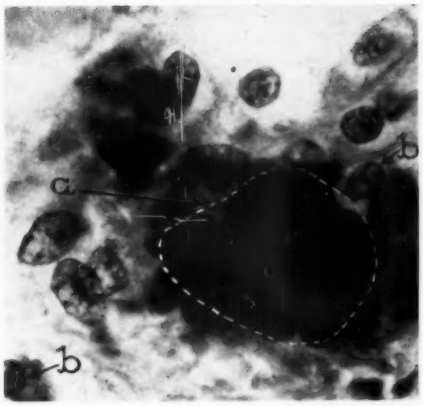

Fig. 2. *Coalescing stage.* Section of renal pyramid which clearly demonstrates a plaque which is made up by the coalescence of many droplets, each containing calcareous material. The outline of all the droplets can still be seen. In some the cell outline is still visible. *a*, The microscopic calculus about the border of which can be seen the outlines of the droplets. *b*, Phagocytes containing bits of blue-black calcareous material. ×920.

the cortex or medulla of the kidneys from 1,500 necropsies. In most of the cases a single section of each kidney was studied microscopically, the section containing a portion of cortex, medulla, and renal papillae. He reported 12 per cent as showing microscopic calcium deposits. He felt that microscopic calcium was more likely to be deposited in the cortex than in the medulla or papillae.

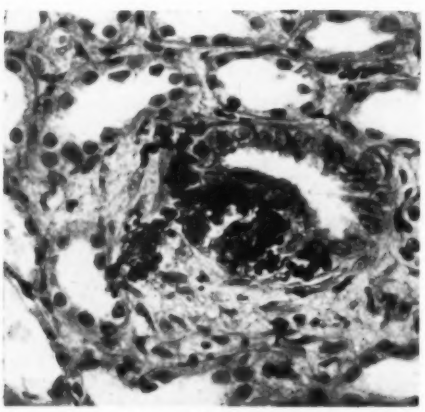

Fig. 3. A tiny calculus which is situated just outside the tubule and seems to be pressing on the still intact lumen of the tubule. ×310.

In 1940, Rosenow reported a study of the kidneys from 209 consecutive necropsies performed at the Mayo Clinic. Particular search was made for the grossly visible patch on the tip of the papillae. He then selected 24 papillae which did *not* show evidence of gross plaque formation and studied these histologically. Only 4 of the 24 papillae showed intramedullary calcification.

Kjølhede and Lassen examined 135 kidneys removed at necropsy and stated that in 49 of the cases neither macroscopic nor microscopic examination revealed deposits of calcium in or on the papillae.

Posey studied the papillae of 340 kidneys removed at necropsy and noted microscopic deposits of calcium in several of the cases.

ORIGIN OF MICROSCOPIC CALCULI

Calcareous deposits stain bluish black with hematoxylin and eosin. The lesions under discussion are not of sufficient size to require decalcification, since they fix and section easily and are visible under the low-power microscope (×100). Photomicrographs are shown to illustrate the lesions.

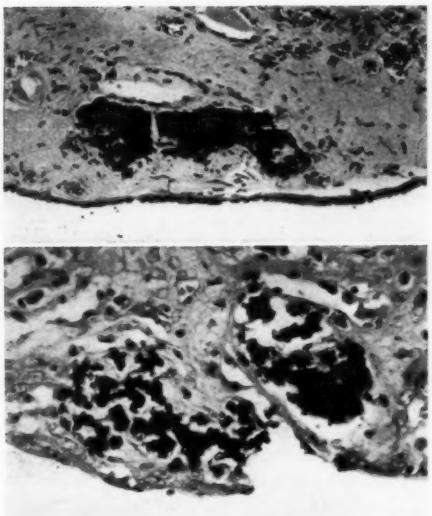

Fig. 4. *Amorphous stage.* a, above, This microscopic calculus is located just under the epithelium at the tip of the renal pyramid. It is almost completely amorphous, showing none, or very little, of the outline of the original droplets. It is situated where it might easily ulcerate through, remain attached, and form the nidus on which the supersaturated salts of the urine of the calices might be deposited. ×130. b, The epithelium overlying the calculus has been eroded away and the area is exposed to the urine of the calices. ×245.

Since these deposits were not described completely in any of the literature that we read, the morphology and apparent developmental cycle of the plaques are outlined in this discussion in some hitherto unused terminology. These terms include "flecks of calcareous material," "droplets," "ingestion stage," "coalescing stage," and "amorphous stage."

Ingestion stage. Phagocytic cells, which are probably macrophages, are abundant about the tubules of the kidney. Kirkman has made an excellent review of the work done on macrophages in the kidney. Phagocytes are shown in Figures 1*b* and 2*b*. Bits of blue-black staining material can be seen in the cytoplasm of the cells. In Figure 1*c* and *c'* can be seen "flecks" of calcareous material which have not yet been ingested by the phagocytes. This may be a result of the cohesion of reabsorbed calcium salts, since there is a concentration of calcium about the kidney

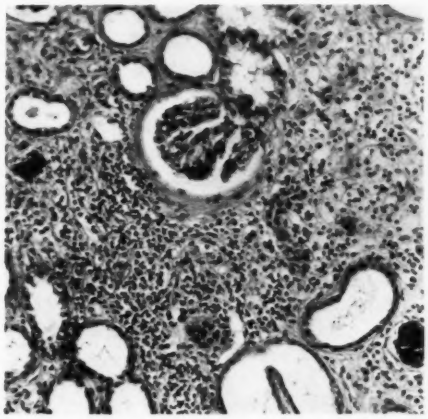

Fig. 5. Microscopic calculi in the renal cortex. ×120.

tubules. The "ingestion stage" refers to the process of ingestion of "flecks" of calcium by the phagocytic cells, which are probably macrophages. This is assumed to be true on the basis of what is demonstrated many times in the sections used in this study, such as that shown in Figure 1.

Coalescing stage. These "droplets" of calcareous material clearly coalesce to form plaques. The still remaining borders of the many tiny droplets which went to make up the plaque can be seen still present about the borders of a high percentage of the plaques (Figs. 1*a*, 2*a*, and 3).

Amorphous stage. It appears from the study of many sections that the tiny calculus tends to become amorphous, losing the semicircular outline of the original droplets which went to make up the entire plaque. Such a calculus is illustrated in Figure 4a.

Subepithelial calculi. Figure 4a shows an amorphous plaque located just under the epithelium at the tip of the renal papilla. This is of the type which Vermooten has suggested may ulcerate through the epithelium and form the nidus for a stone according to Randall's hypothesis of formation of stone.

Figure 4b demonstrates the ulceration of the epithelium by a calculus which originated just under the epithelium. The calculus has ulcerated or eroded away the epithelium, thus exposing the plaque to the salts of the urine.

TABLE I.—RESULTS OF THE COMPLETE STUDY ON THE GROSSLY NORMAL AND THE SURGICALLY REMOVED DISEASED KIDNEYS AS TO FREQUENCY OF THE MICROSCOPIC CALCULI

Type of kidney	Kidneys	Average number of sections per kidney studied to prove the presence of the microscopic calculi	Total number of sections made
Pyelonephritic	57	3.71	212
Hydronephritic	36	3.71	133
Calculous	31	3.83	120
Tuberculous	24	3.84	92
Grossly normal	20	3.60	72
Total	168	3.74	629

All patients were 9 years of age or more. All kidneys showed the lesions.

Cortical calculi. The cortex of the kidney was not intentionally included in this study but, in cutting pyramids, the tissue of the cortex was frequently included. The interpretation placed on the finding of the calculi about the glomeruli is that reabsorption of calcium may occur in any part of the tubular system, which includes of course the convoluted tubules.

Vermooten expressed the belief that these calcareous deposits occur in the collagen fibers of the renal papilla. With this, we would have no argument except to point out that to us they seemed to occur anywhere (Fig. 5) except within the lumen of the tubule. A few specimens were found with the deposits within the tubules but it seemed to us that they had eroded into the tubule from the surrounding parenchyma. Caution must be observed in the interpretation of location since the studies in three planes which would have been afforded with serial sectioning were not used. Figure 3 shows a calculus which is outside the lumen of the tubule but seems to be pressing into the lumen and perhaps in time would have eroded its way into the tubule itself. It would have then been exposed to urine and might have grown to form an interparenchymal stone.

Randall, Vermooten, and Rosenow have very carefully followed the fate of the plaque after it appears grossly visible while attached to the tip of the renal papilla. That study is not a part of this work. *Macroscopic* plaques which were attached to the tip of the renal papilla were observed but their frequency was not recorded.

FREQUENCY OF THE DEPOSITS

The results of the study as to frequency of the deposits are shown in Table I. On the average, it was necessary to cut and study fewer than 4 histologic preparations on each kidney to prove the presence of the microscopic calculi in all of the kidneys. As many as 10 sections of some kidneys were cut before the lesion was found but in more than 50 per cent of the kidneys the calculi were found in the first section studied. We conclude that these microscopic calculi probably occur in the kidneys of all people above the age of 10 years. Kidneys from the very young were not made a part of this report. The age varied from 9 years to 79 years with a mean of 43 years.

It is interesting to note in passing that the conclusions of this work were arrived at by studying an average of 1/3,333 part of the total pyramid area of each kidney. This figure is easily deduced from the information that each section is only 10 microns (0.001 cm.) in thickness and the knowledge that each kidney contains about 10 pyramids, each of which is about 1 centimeter thick. To study all of the papillary area of only one kidney might require as many as 10,000 sections. However, this would probably not be necessary in actual practice, since the calculi probably extend over the thickness of many sections.

SIGNIFICANCE

Certain generally accepted postulates regarding the physiology of the kidney will be correlated with the findings of this work in suggesting an interpretation of the causation of kidney stones. These postulates will be defended by references to the work which has been done on physiology and pathology of the kidney.

Postulate 1. The concentration of calcium (and related ions) is high in the tissue fluid about the renal tubules.

Postulate 2. Phagocytic cells occur in abundance about the renal tubules. Most work indicates these to be macrophages. Macrophages have been shown to have a definite affinity for calcium.

Findings. (1) Phagocytic cells are demonstrated in the process of ingesting calcium in the renal pyramid (Fig. 1*b*, ingestion stage). (2) "Flecks" of calcium are shown about the renal tubules. These flecks are apparently outside the walls of any cells. (3) "Droplets" of calcium are shown within the confines of still present phagocytic cell membrane (Fig. 1*d*). (4) Small calcareous plaques are shown, about the edge of which can still be seen the rounded borders of the many droplets which went to make up this coalesced deposit (Fig. 1*a*, coalescing stage). (5) These microscopic calculi were found in all of the kidneys. The patients were all 9 years of age or more. The lesions were sometimes found in the first section made on a kidney. Sometimes as many as 10 sections were necessary to demonstrate this finding. On an average something more than 3 sections were made on each kidney. Six hundred and twenty-nine sections were made of 168 kidneys. (6) Amorphous calculi were found which had entirely lost the outline of the original "droplets" or cells (Fig. 4a, amorphous stage). (7) Subepithelial calculi were found which had entirely lost the outline of the original "droplets" or cells and were located just under the epithelium at the tip of the renal pyramid (Fig. 4a). (8) Deposits were found eroding through the epithelium at the tip of the papilla and yet remaining fixed to the papilla (Fig. 4b).

Interpretation. (1) The study suggests that these microscopic calculi occur in practically all people, as a result of the physiologic process of phagocytic ingestion of the reabsorbed calcium by the kidney tubules. (2) Renal calculus may be a systemic or a dietary disease and not a disease of the kidney *per se*. This assumption follows from the fact that, although this tiny calculus, which may act as a nidus, is present in practically all people, not all people have symptomatic renal calculi. The finding of the tiny calculi in the process of ulcerating through the epithelium at the tip of the renal papilla and yet remaining firmly fixed to the papilla and bathing in the salts of the urine of the calices and receiving deposits therefrom would seem to substantiate the findings of Randall, Vermooten, and others that these plaques may form the nidus of renal calculi. This seems especially striking when it is considered that only a small part of the actual pyramidal area of each kidney was actually studied in this work (1/3,333) and yet all kidneys were found to have these tiny microscopic calculi. The answer may lie outside the kidney itself. We may suppose that some substance appears in the urine or blood which acts as a catalyst to the formation of a stone of sufficient size to cause symptoms, this catalyst causing the salts of the urine to be precipitated on the aforementioned nidus. Perhaps the unknown substance causes the epithelium to ulcerate, thus exposing the plaque to the urine. Really, most microscopic calculi are subepithelial. The formation of symptomatic calculi could be due to the absence of some vitamin-like substance or the presence of some other unknown or known substance from the general metabolism of the body or from the diet.

Defense of postulates. Postulate 1 is that the concentration of calcium (and related ions) is high in the tissue fluid about the renal tubules. Practically all of the blood supply of the tubular system of the kidney consists of blood which has previously passed through the glomerulus. Cowdry and Shonyo and Mann have made exhaustive studies of the vascular tree of the kidney by the injection-corrosion technique and have demonstrated that practically all of the arterial blood reaching the capillaries surrounding the different parts of the tubules is blood which has passed through the glomerulus before it reaches the renal tubules. That there are a few exceptions is not to be denied but that these few exceptions constitute a very small part of the tubular circulation seems also well substantiated. Therefore the *efferent* arterioles of the renal glomerulus carry blood which is soon to pass close to the epithelium of the entire tubular system clear down to the end of the collecting tubules at the tip of the renal papillae.

The function of the glomerulus, it seems well proved by the work of Richards, is to filter off by selective osmosis a protein-free filtrate of the blood plasma. The constituents of the glomerular filtrate are grouped into three classes: (a) high threshold substances which are actively reabsorbed (sodium, po-

tassium, calcium, magnesium, and chlorine); (b) low threshold substances; and (c) non-threshold substances. For the purposes of this paper we are not interested in the last two classes.

The high threshold substances are in low concentration in the urine and in high concentration in the reabsorbed fluid. This conclusion is drawn from the following reasoning: Richards pipetted off the glomerular filtrate and found that it consisted of a simple protein-free filtrate of the blood plasma. As blood passes through the glomerulus, it forms concentrated blood, which passes out of the kidney through the efferent arteriole, and glomerular filtrate, which starts down the tubular system. Two elements of the blood in the first part of the efferent vessels will now be in higher concentration; namely, the cells and the proteins. The other substances have simply filtered across the osmotic membrane of the glomerulus and remain in the same concentration in the glomerular filtrate as in the blood of the efferent arteriole. The concentration of these ions is therefore unchanged in either. The blood now starts its way down the efferent vessel and passes beside the tubules where the high threshold substances are reabsorbed. Therefore the concentration of these high threshold ions should be high in this blood. Also, if the concentration of these easily diffusible ions is the same in tissue fluid as it is in the plasma, the passage of these ions from the glomerular filtrate mentioned previously should increase their concentration in the tissue fluid in the cells and tissues about the tubules as it is reabsorbed. Of course, much of the water is reabsorbed along with the ions but some must go out to form urine. This is estimated to be about 1 cubic centimeter of urine for every 100 cubic centimeters of glomerular filtrate.

Most anatomists and histologists today feel that reabsorption takes place in the convoluted tubules and in the loop of Henle but not down in the tubules of Bellini. Their assumption is largely based on the histologic appearance of the epithelium in the tubules of the collecting type. The epithelium is flattened and undifferentiated in appearance. It does not appear like epithelium elsewhere in the body which does carry on active reabsorption. However, the pyramids contain the lowermost pole of the loop of Henle. As Lowsley and Kirwin stated, "The pyramids are composed of Henle's loops and the straight collecting tubules." We see that reabsorption by the straight collecting tubules is not essential to the completion of the hypothesis and would not be in disagreement with the finding of calcareous plaques well down at the papillary tip. Perhaps the straight tubules do carry on some of the functions of reabsorption.

The question may arise as to the real significance of this supposed high concentration of calcium near the tubules. Some may feel that this concentration is not much higher in actual milligram equivalents than the increase in concentration which occurs with the daily variations of the alkaline tide. Perhaps this is true but it must be pointed out that the concentration of reabsorbed calcium would probably be even higher at this high peak of the day. Perhaps this is exactly the time when the phagocytic cells do absorb the particles of calcium.

Postulate 2 is that phagocytic cells, which seem to be macrophages, occur in abundance about the renal tubules and that macrophages have been shown to have a definite affinity for calcium. A complete review of the subject of macrophages in the kidney is to be found in the work of Kirkman published in 1943. Kirkman also studied the kidneys of rats 25 days of age. The average number of macrophages per square millimeter throughout the pyramid, medulla, and cortex respectively was 53, 93, and 14.

Gersh, in 1938, studied the liver and noted that macrophages of the liver as well as those of the spleen had a special affinity for calcium compounds.

Our final interpretation of this study is that in the process of reabsorption of high threshold substances (calcium and related ions) these substances are engulfed by phagocytic cells, which may be macrophages. These ions may first cohere in small masses or "flecks," as shown in Figure 1, before being engulfed by the individual macrophage. Soon the cell contains so much of the metal that it loses its

identity and forms spherical droplets. By cohesive attraction these droplets come together in groups to form a tiny calculus or plaque, which we have chosen to call a microscopic calculus. The outlines of the droplets which came together to form the calculus can still be seen about the border of the lesion. Finally, all identity of the original droplets is lost in the amorphous plaque. We conclude that this occurs in practically all kidneys. If, then, these tiny calculi are present in everyone and are found ulcerating through the epithelial membrane of the papillary tip in as high a percentage as is suggested by Randall, Vermooten, and Rosenow, why does not symptomatic renal calculus occur more frequently? We feel that perhaps the inciting factor may lie outside the kidney itself and may be a systemic or a dietary factor.

When this calcareous plaque of the type occurring in almost everyone breaks through the epithelium at the papillary tip, it is exposed to the bathing salts of the urine and thus may form a layered concretion or stone, which may ultimately break loose and form a symptomatic calculus. That urinary calculi consist predominantly of more than one component is confirmed by Thompson and his associates and by Higgins. This fact lays the foundation for supposing that this microscopic calculus may well serve as the nidus for any type of stone, whether it be oxalate, urate, xanthine, cystine, carbonate, or phosphate, when the proper inciting factor comes along.

SUMMARY

A study was made of microscopic calculi as found in the pyramids of 168 kidneys. These included surgically removed kidneys and grossly normal kidneys removed at necropsy. The diseased kidneys were removed for tuberculosis, hydronephrosis, pyelonephritis or stones. Six hundred and twenty-nine histologic preparations were made. Originally only one hematoxylin and eosin section of each kidney was studied. Failure to find the microscopic calculi after study of the section from any particular kidney was followed by the cutting and section of further pyramids from the same kidney until the plaques were found or their absence was proved beyond a reasonable doubt. All of the kidneys were from patients more than 9 years of age. In 50 per cent of the kidneys the plaques were found in the first section studied. In some kidneys, as many as 10 histologic preparations were made. The microscopic calculi were found in all of the kidneys.

These microscopic calculi were studied as to morphology and possible histogenesis. It was demonstrated that they were formed by the coalescing of numerous "droplets" of calcareous material. These droplets seemed to be formed by the process of phagocytic ingestion of tiny "flecks" of black-staining material. Attention was directed to the postulate that the concentration of calcium is probably high in the tissue fluid about the renal tubules and to the fact that phagocytic cells occur in abundance about the renal tubules. From these data it was suggested that the calculi were formed by the process of phagocytic ingestion of the calcium which is reabsorbed by the renal tubules.

It was shown that the tiny calculi occur throughout the renal parenchyma. Some were located just under the epithelium at the tip of the papilla and one photomicrograph demonstrated the plaque ulcerating through this epithelium and becoming exposed to the urine of the calices. It is now fairly well accepted that some renal calculi are formed by the process of the salts of the urine being deposited in layers on these plaques. Since a chemically pure calculus is very rare, the suggestion is made that perhaps many different types of stone may have this tiny calculus as a nidus.

Since these microscopic calculi occur in practically all people, even though only 1/3,333 part of the total pyramidal region of each kidney was cut and examined, the question was raised as to why then do not more people form symptomatic stones. The interpretation was suggested that large stones may form only when some inciting factor comes to the kidney which causes the salts to deposit on this eroded nidus plaque. Perhaps this inciting factor, substance or catalyst, the absence or presence of which is necessary to cause deposition to occur, comes from outside the kidney. From the foregoing data the pro-

posal was made that perhaps renal calculus is a systemic or a dietary disease and not a disease of the kidney *per se*.

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RESECTION OF THE RECTUM WITH RECONSTRUCTION OF CANAL THROUGH THE PERINEAL APPROACH

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RESECTION of the rectum with reconstruction is presented as an alternative method of dealing with some lesions of the rectum. The abhorrence of a colostomy by some patients when they are told they have a cancer of the rectum is sufficient to decide them against having operation. The surgeon as well may have some qualms regarding the operation of abdominoperineal resection of the rectum for some reason such as early malignancy, small malignant polypi, ulcers which are of doubtful nature, etc. If a smaller operation without colostomy and good prospects of a return of function would suffice, it would place both the surgeon and patient in a happier frame of mind.

The investigations of Davis and Coller have shown that if a carcinoma of rectum or sigmoid has metastasized beyond the pararectal lymph nodes, the next extension may just as well be in the liver or some remote region, as in the next lymph node, namely the intermedial or central groups. Therefore, it is reasonable to believe that, if there are no metastases beyond the paracolic lymph nodes, adequate excision of the colon including the primary lesion together with the epicolic and paracolic lymph glands offers almost as good a prognosis for cure as does a wider resection including the intermediate and central lymph nodes.

With that belief in mind, it was considered that in certain selected carcinomas in the rectum, which are not fixed to surrounding structures, which are not producing obstruction, which have produced no obvious metastases, and which are either a cauliflower or an ulcerative type of lesion, involving not more than one-third to one-half of the circumference of the rectum, a local resection and reconstruction might have many advantages. These advantages might be: (1) normal rectal and anal sphincters would be retained with subsequent normal control of the bowels; (2) no colostomy would be required; (3) the shock of operation would be greatly diminished; (4) the danger from infection would be diminished; (5) postoperative complications would be greatly reduced.

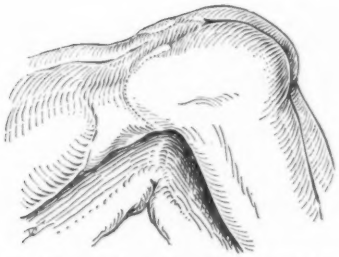
A group of patients have been treated in this way and the case reports are presented.

To select the cases suitable for this procedure, it has finally been decided that the ideal case is one in which the growth is above and not involving the sphincters or anal canal mucosa. The growth should be easily palpable through the rectum and for a transacral resection the upper margin of the growth must be palpable with the finger in the rectum, and be freely movable on surrounding structures.

OPERATIVE TECHNIQUE

An incision is made from the third spine of the sacrum down to within half an inch of the posterior anal margin. The coccyx, the fifth, and half of the fourth sacral bodies are removed. The pelvic fascia is divided. The dissection is carried around the circumference of the rectum outside the pararectal fascia. When a tape has been placed around the rectum, gentle traction and digital dissection will draw down the upper portion of the rectum and sigmoid. The peritoneum is opened on the anterior surface and sufficient sigmoid is drawn down with which to do a repair with the remaining lower structures of the rectum. When this has been accomplished, the peritoneum is reattached by sutures to the anterior wall of the sigmoid at a new level higher up. The field is then well dusted with sulfathiazole powder and after the field is thoroughly packed off, the rectum is opened well below the growth which is palpable within the lumen. On inspection through this opening, if the growth is not within 1½

From the Toronto General Hospital and the Department of Surgery, University of Toronto.



Position of patient on table

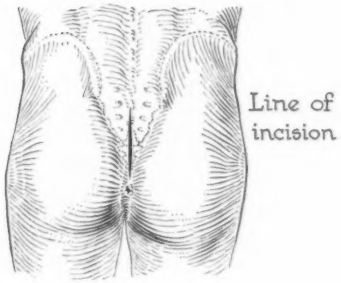


Fig. 1.

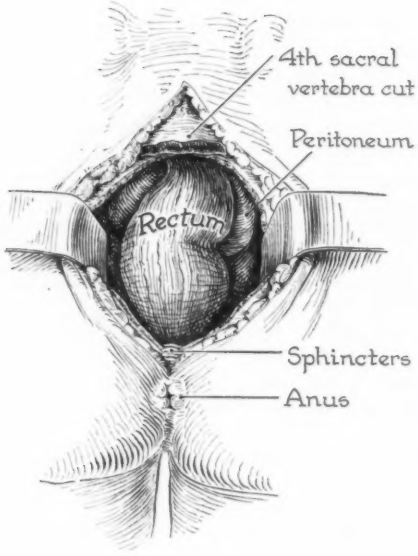


Fig. 3.

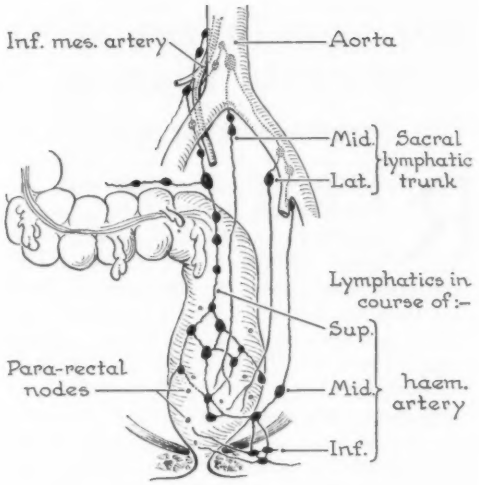


Fig. 2.

inches of the site of section, the rectum is divided completely across. The sigmoid is divided across well above the growth and this section of rectum with its surrounding para-rectal fascia, lymph glands, and lymphatics with the contained growth are removed. It is an easy matter then to do an end-to-end suture between the lower end of the divided sigmoid and the upper end of the remaining rectum. The suture material used has been chromic catgut. A single layer of full thickness sutures has been used. Over the posterior surface some supporting sutures in the fat and surrounding structures have also been applied.

A soft drainage tube is passed down to the cavity below the tip of the sacrum. The levatores ani are closed and if some of the fibers of the sphincters of rectum have been divided these are repaired and the skin closed. Digital examination will now demonstrate the suture line surrounding the rectum and a hard rubber tube 5/8 inch in diameter is passed through the anal canal, through the site of anastomosis, and into the proximal segment. This is stitched to the anal margin. No colostomy is required.

There have been no fatalities in this group. The patients stood the operation without shock and within 2 or 3 days were feeling

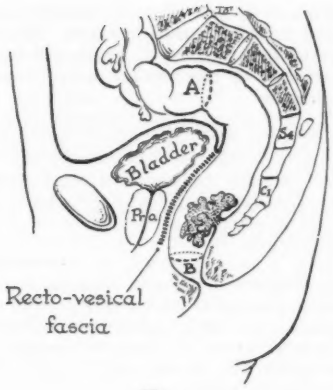


Fig. 4.

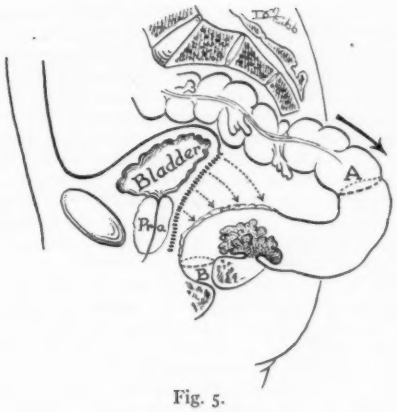


Fig. 5.

quite normal. There has been no peritonitis, or other serious complications. All the patients have had control of the rectum. There has been serous discharge from the sacral drainage in all and in some there has been suppuration with purulent discharge, but in most this has healed. There has been no osteomyelitis of the sacrum. There has been no stenosis. In 1 case in which the growth was slightly higher up so that its upper margin could be scarcely felt, there was slightly more tension than is advisable at the suture line. In this case the patient developed a fecal fistula which discharged through the site of the sacral drainage tube for 10 days. It then closed spontaneously without further complications. The patient made an excellent recovery and has normal function of the rectum. In another patient in whom there was a larger growth requiring resection of a greater length of rectum and which probably was not suitable for this procedure, there was a separation of the suture line around half of the circumference of the rectum. A fecal fistula developed and has persisted for 4 months, through which a small quantity of feces discharged daily.

What the end may be is not known and a colostomy may be necessary before the condition is cleared up. In half the cases, a temporary fecal fistula developed, but this healed spontaneously with 1 exception within 3 weeks. In none of the cases was a colostomy performed.

CASE REPORTS

CASE 1. O. M., female, aged 65 years, was admitted to the hospital March 9, 1942. For 3 months this patient had had rectal bleeding. On digital examination her doctor found a small mass 1¾ inch in diameter, 3 inches within the rectum. Biopsy showed this to be adenocarcinoma. Three inches of rectum, proximal and distal, including the growth were excised and an end-to-end repair carried out. The specimen showed no invasion of regional lymph nodes. The patient was discharged on March 24, 1942. The incision had healed. There was normal control of the rectal sphincter and colon function was normal in all respects.

This patient is still well without signs of recurrence and with normal function now 3 years following the operation.

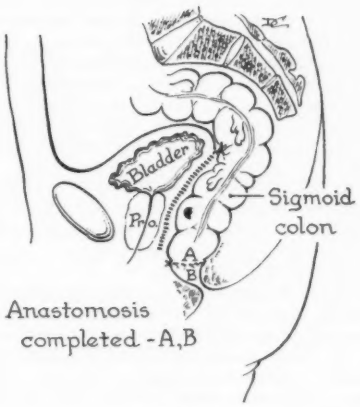


Fig. 6.

CASE 2. A. H., aged 35 years, was admitted to the hospital on March 22, 1942. The patient had typical symptoms of carcinoma of rectum which were demonstrated on digital examination. He had lost 30 pounds in weight. There was marked secondary anemia with a hemoglobin of 54 per cent. He was sleeping poorly and was in constant distress from the rectal lesion. A large mass surrounding two-thirds of the circumference of the rectum, ulcerated in its center was easily palpable. It extended downward beneath the mucosa of the anal canal on the posterolateral aspect. The mass was not fixed to surrounding tissues.

Through a sacral approach, the rectum was exposed. It was demonstrated on palpation that the mass was extending in the submucosa deep to the external sphincter of rectum. The question arose whether an adequate resection could be carried out locally or whether an abdominoperineal resection would improve the prospects of cure. It was felt, however, with the possible muscle invasion that the prospects for cure under any condition were not good. A local resection was carried out when the posterior half of the rectal and anal sphincters together with rectum and growth were removed. An area of anal mucosa 2 inches by 1 inch was left on the anterior wall. The anal canal was reconstructed and the external sphincter reconstructed around this. The lower end of the sigmoid was anastomosed to the end of anal canal. Microscopic studies demonstrated this growth to be an adenocarcinoma with invasion of regional lymph nodes. The patient made an uninterrupted recovery and left hospital with the incision healed in 2 weeks. There was normal control of the anal and rectal sphincters and the patient had normal colon function.

The patient's general health improved and he returned to work. He returned in 5 months complaining of pain in the region of the left hip. X-ray films at that time showed an area of rarefaction in the femur which had the appearance of a metastatic growth in bone. While the patient continued at work for a year, this growth in the femur enlarged until finally there was a pathological fracture. The patient finally succumbed to generalized metastases of peritoneal cavity and skeleton. There was a small local recurrence of the growth in the anal region during the last few months. With local radiation this was controlled and caused no further symptoms.

It is doubtful if a more radical operation would have made any difference to the incidence of metastases as these almost certainly were present before the operation.

CASE 3. J. B., aged 70 years, was admitted to the hospital in August, 1941. The patient had a malignant polyp 2½ inches in diameter on the posterior wall of the rectum 2 inches from the anal margin.

Through a posterior approach the involved segment of the rectum with 2 inches distally and 3 inches proximally was excised together with the lymphatics and lymph glands. Sulfathiazole was applied and a drainage tube inserted. The skin incision was healed in 10 days. There was no fistula. The suture line in the rectum healed completely without stenosis.

The patient has normal control of the bowel and rectum. Analysis of the specimen showed it to be polypoid adenocarcinoma. There were no metastases in the regional lymph glands removed.

CASE 4. C. S., aged 58 years, was admitted to the hospital on September 4, 1942. This patient had an ulcerating carcinoma in the anterior wall of the rectum beginning 1½ inches above the sphincter region. The growth was 2½ inches in length by 1¾ inches in width. It moved fairly freely over the vaginal wall anteriorly.

Through the posterior approach the mass with 3 inches of the rectum proximally and 2 inches distally was removed together with the surrounding fat, fascia, lymphatics, and lymph glands. An end-to-end suture was carried out without difficulty. The suture line was completely healed within 3 weeks. There was no fistula. The patient had normal control of bowel and rectum. There was no stenosis on examination. Dissection of the specimen showed this to be an adenocarcinoma with invasion of the epicolic but not of the more remote lymph nodes.

Now 2½ years following the operation there is no evidence of recurrence either locally or generally.

CASE 5. E. T. O., aged 62 years, was admitted to the hospital on October 18, 1943. A malignant polyp 2½ inches in diameter attached to the anterior wall of the rectum was identified. Biopsy described this as a polypoid carcinoma.

Through a posterior approach a length of 6 inches of rectum and lower sigmoid was removed with the surrounding lymphatics and lymph glands with the growth in the center. An end-to-end suture was carried out without difficulty. A drainage tube was passed down to this area. The suture line was completely healed in 2½ weeks. There was no fistula. The patient had normal control of the rectum and bowels. The suture line was healed satisfactorily. There was no stenosis. There was no evidence of recurrence either locally or generally 1¼ years following the operation. Sections of the specimen showed no invasion of regional lymph glands.

CASE 6. E. B., aged 72 years, was admitted to the hospital on December 15, 1943. The patient had an adenocarcinomatous ulcer in the posterior wall of the rectum 4 inches from the anal margin. There was no evidence of metastases.

Through a posterior approach the involved segment of rectum with 3 inches of colon proximally and 2 inches distally was removed with surrounding fat, lymphatics, and glands. This was at the upper

margin of the point at which the resection by this method could be carried out. However, a satisfactory end-to-end repair was completed, although there was somewhat more tension at the suture line than was desirable. The patient developed a fecal fistula which lasted for 10 days, at which time it healed. The skin incision was completely healed in 3 weeks. The patient had normal control of bowel and rectum. There was no stenosis and no evidence of new growth 1 year following the operation. Analysis showed this to be adenocarcinoma involving the muscular coats and with no invasion of regional lymph glands.

CASE 7. A. D., aged 60 years, was admitted to the hospital on January 7, 1944. This patient had symptoms typical of carcinoma in the rectum. On examination there was an ulcerated area on the posterior wall, the growth measuring 3.5 centimeters in diameter. It was freely movable and it was thought that it was suitable for a local resection.

Through a posterior approach, the rectum with the pararectal fascia, lymphatics, and adjacent lymph glands was dissected free. Seven inches of the lower sigmoid and rectum was removed with the malignant mass in its center. An end-to-end suture was carried out without difficulty giving a satisfactory repair. Sections of the specimen showed it to be an adenocarcinoma with metastases in the paraepicolic lymphatics but none in the immediate lymph glands which were removed. The incision was healed completely in 2 weeks. There was no fistula.

To date there is no evidence of recurrence. The patient has normal function of the bowels and control of the rectum.

CASE 8. A. O'G., aged 52 years, was admitted to the hospital on June 7, 1944. The patient had a malignant ulcer on the posterior wall of the rectum 4½ inches from the anal margin.

Through a posterior approach the involved segment with 2½ inches proximal and 2½ inches distal was removed. An end-to-end suture was carried out satisfactorily. The posterior incision was healed completely in 2 weeks. There was no evidence of fistula. The bowels and rectum were functioning normally. Analysis of the specimen showed this to be only a chronic ulcer which differed from the original biopsy. There was no evidence of malignancy. There was no primary or invasion in the regional lymph glands.

CASE 9. A. N., aged 58 years, was admitted to the hospital on August 11, 1944. The patient had an ulcerated carcinoma in the posterior wall of the rectum 3 inches above the anal margin. It was lightly attached to surrounding structures, especially on the right posterolateral quadrant. There was no evidence of metastases elsewhere.

Through a posterior approach the involved segment of the growth with 2 inches proximally and 3 inches distally was removed. A satisfactory end-to-end repair was carried out. However, there was more tension in the suture line in this case than was desirable. Sulfathiazole was applied and a drainage tube was passed down to the site. The patient developed a fecal fistula on the eighth day which discharged a moderate amount of feces through the upper end of the incision. In the meantime the bowels were functioning naturally. On palpation through the rectum the posterior half of the suture line had separated leaving a gap of 1½ inches between these margins. The fistula continued to discharge small quantities of feces. Otherwise there was normal control of the bowels.

Now 7 months following the operation there is still a small fecal fistula over which the patient wears a small layer of gauze. Otherwise the bowels are functioning normally. The patient's general health is excellent. There is no evidence of recurrence of the growth. Analysis of the specimen showed this to be adenocarcinoma. The glands removed from the perirectal area showed only chronic lymphadenitis with no evidence of new growth.

CASE 10. M. M., aged 62 years, was admitted to the hospital on August 11, 1944. The patient had a carcinomatous ulcer 2½ inches in diameter in the posterior wall of the rectum 3 inches above the anal margin. It was fairly freely movable but still it was felt that there was slight attachment to the surrounding structures, especially on the left posterolateral region. There were no evidences of metastases elsewhere.

Through a posterior approach the involved segment of rectum with 3 inches proximally and 2 inches distally was removed. The surrounding fat, lymphatics, and lymph glands were removed. A satisfactory end-to-end repair was carried out. Sulfathiazole was used, as in all these operations, and a drainage tube was passed down to the site. The incision was completely healed in 2½ weeks. There was no fistula at any time. The patient had normal control of bowel and rectum. There was no stenosis on digital examination. The analysis showed this to be an adenocarcinoma. The regional lymph glands in the pararectal position showed no invasion by carcinoma.

CASE 11. T. F., aged 64 years, was admitted to the hospital in August, 1944. This patient had a polypoid carcinoma on the posterior wall of the rectum 4 inches from the anal margin. There was no evidence of fixation of the growth.

Through a posterior approach the affected segment with the growth with 3½ inches proximally and 2½ inches distally was removed. A satisfactory end-to-end repair was carried out. At no time was there a fistula. The incision was healed in 10 days. The patient had normal control of bowel and rectum. There was no stenosis. The analysis of the specimen showed this to be an adenocarcinoma. There was no

evidence of invasion of regional lymph glands.

CASE 12. M. T., aged 21 years, was admitted to the hospital on October 10, 1944. The patient had symptoms leading to the diagnosis of rectal polyp. On biopsy this was shown to be a malignant polyp on the posterior wall of the rectum within an inch of the anal mucosa. This growth was treated in the radiology department by deep therapy and interstitial radium application. The lesion appeared to be cured by this procedure. However, it left the patient with a radiation ulcer 1¼ inches long and ¾ inch wide in the posterior wall of the rectum extending down into the region of the sphincter posteriorly. As this had persisted for a year and a half and was causing a great deal of discomfort and disability, it was suggested that an excision of this area be carried out.

On October 10, 1944, the area was exposed through a posterior incision. The circumference of the rectum was defined and the area of ulceration localized. The posterior two-thirds of the circumference of the rectum was excised by an elliptical incision including the ulcer. This was repaired with a double line of sutures. A drainage tube was passed down to this site after applying sulfathiazole crystals. Healing was quite satisfactory and was completely closed in 3½ weeks. The symptoms were entirely relieved. On rectal examination the suture line was palpable. It was well healed.

CASE 13. I. W., aged 55 years, was admitted to the hospital on November 13, 1944. This patient was demonstrated 6 months previously to have carcinoma of the rectum. It was adherent to surrounding structures. It was treated by the radiologists with deep therapy and with interstitial radium. The growth diminished in size leaving only a scarred area causing fairly severe stenosis 3 inches above the anal margin. He was seen in consultation with the radiologists when it was decided to make an attempt to resect this segment of the invaded rectum.

Through a posterior approach it was demonstrated that there was much more scarring in the tissue surrounding the rectum than was found under ordinary conditions. probably as a result of the radiation therapy. However, it was not difficult to define a plane through which a dissection could be carried out surrounding the rectum, pararectal fascia, lymphatics, and adjacent lymph nodes. The involved segment of rectum with 2½ inches proximally and 2 inches distally was removed. An end-to-end suture was carried out without difficulty. The incision was somewhat slower in healing. This might have been the result of the previous radiation. However, it was healed satisfactorily in 4½ weeks. A fistula discharging only a small quantity of feces developed for a period of 3 weeks. This finally closed. The patient had normal control of bowel and rectum and there were no symptoms. The analysis of the specimen removed showed that there were still carcinoma cells in the region imbedded in massive scar tissue. The lymph glands removed with the rectum showed no invasion by carcinoma.

CASE 14. G. T. B., was admitted to the hospital in March, 1945. This patient clinically had carcinoma palpable with the tip of the finger on the anterior wall of the rectum. It was felt to be moderately large and probably not very suitable for a perineal excision. However, as the patient was firmly decided against having a colostomy, it was decided to attempt removal by the perineal approach.

At the operation it was found that the mass was fairly large, although there was no extension to lymph glands beyond the regional group which could be identified at operation. The mass was removed. The repair was carried out without much tension. A tube was passed through the anastomosis and post sacral drainage provided. The patient stood the operation very well. The incision healed without infection. There was a slight fecal discharge for about 1 week. By the end of 2½ weeks the incision and the fistula were completely healed. The patient had complete control of the sphincters at that time. There was no stenosis present at the suture line and the patient made a satisfactory recovery.

The pathologist's analysis of the specimen showed this to be an adenocarcinoma of colon. The regional lymph glands showed no invasion by secondary growth. They showed only chronic lymph adenitis.

CASE 15. C. C., aged 64 years, was admitted to the hospital in May, 1945. In 1931 this patient had had an operation for internal hemorrhoids at another hospital. A polypoid mass 1¼ by 1½ inches was removed. On section this was demonstrated by the pathologist at that time to be adenocarcinoma. The patient was quite free from symptoms until January, 1945, at which time he began to have symptoms typical of carcinoma of rectum. On examination there was a polypoid mass which was situated in a position on the anterior and left lateral wall of the rectum where it could be palpated with the finger freely but its upper margin could not be felt easily. There was one unpleasant symptom which was irritation of the bladder, making one doubt if this growth were resectable. It was decided to attempt an exploration through the perineum, being prepared to continue to do an abdominal stage if the growth were not removable through the former route. It was found that the growth could be quite freely detached from all the surrounding structures. It was brought down into the post-sacral incision without difficulty. It was resected and a satisfactory end-to-end repair was carried out without colostomy. The patient made an uninterrupted recovery. There was a fistula present for about 3 weeks. This healed and left the patient with a normal functioning rectum without any stenosis.

The pathologist's analysis of the specimen showed an adenocarcinoma of fairly large proportions of the cauliflower type but no invasion of regional lymph glands.

CONCLUSIONS

1. In early carcinoma of rectum extending as low as the anal canal, resection with reconstruction and preservation of the sphincters without colostomy is a satisfactory procedure.

2. The operation is attended by very little shock or hemorrhage. The patients all made a satisfactory recovery. There were no deaths in this group reported.

3. This report is based on 15 cases. With the exception of 2 cases, all infection in the perineal wound had healed and signs of fistula had disappeared within 3 weeks. In one of the remaining two, the fistula closed in 5 weeks. In one other it was present at 4 months. What the end-result in this will be is not yet determined. The prospects for cure in this group seemed fairly satisfactory. This was based on the pathologist's evidence that there was no extension of the growth beyond the local lesion with possible infiltration of the surrounding muscular wall. There was 1 lymph gland invasion. All the patients had normal control of sphincters. There was no stenosis at the site of anastomosis. The rectum function was normal in all respects.

4. One patient has died from recurrent growth with metastases in the peritoneum and bone causing a fracture of femur. This case, Case 2, in this series was an unsuitable case, as it was a very advanced carcinoma with invasion of the anal mucosa and surrounding structures. It is quite obvious, however, that any other type of procedure would not have offered any better prospects for cure.

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STUDIES ON EXOPHTHALMOS PRODUCED BY THYROTROPIC HORMONE

I. A Study of Exophthalmos Produced by Various Thyrotropic Hormones and the Influence of the Testes on the Exophthalmos

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MANY investigators have demonstrated that thyrotropic hormone from the anterior pituitary may be used to produce exophthalmos in guinea pigs. Many of the observers have found that the exophthalmos was produced more easily in thyroidectomized than in intact animals. The problem of obtaining accurate measurements of the prominence of the eyes in many of these experiments has been a major obstacle. Two improved methods for measuring minute changes in the prominence of the eyes have been devised and described elsewhere (6).

Using these two methods of measuring exophthalmos, a rather extensive investigation has been undertaken, first, to compare the changes in the prominence of the eyes induced by various preparations of thyrotropic hormone and, second, to correlate the exophthalmos with the various tissue changes which occurred as a result of administration of the hormone. This report not only describes the effects induced by the administration of various anterior pituitary preparations on the prominence of the eyes in guinea pigs but also takes into consideration the influence of the testes on the development of exophthalmos.

The literature dealing with the relation of the gonads to exophthalmos is confusing because of the variety of ways which have been employed to produce exophthalmos. Marine (16-18) and Marine and Rosen (20) reported that exophthalmos did not develop in gonadectomized puberal rabbits as it did in normal animals when thyroid insufficiency was produced by thyroidectomy or methyl cyanide. They (17-21) found that the production of permanent cryptorchism with the associated degeneration and absorption of germinal epithelium of the testes did not inhibit this type of exophthalmos in rabbits. Spontaneously exophthalmic guinea pigs did not show a regression of their exophthalmos after gonadectomy. They reported (21) that these types of exophthalmos could be instantly converted to enophthalmos by cervical sympathectomy. This fact would serve to distinguish this type of exophthalmos from that produced by thyrotropic hormone, which is not influenced by cervical sympathectomy (32, 33, 36). No changes in body weight of the animals resulting from surgical procedures were described.

Smelser (33), reporting studies on exophthalmos induced by thyrotropic hormone, referred to the fact that some of his male and female animals were gonadectomized. Special reference, however, to the results in these animals was not included. Smelser (38) reported that oophorectomy had no effect on the changes that were induced by thyrotropic hormone in the harderian glands of guinea pigs.

Marine (17, 18) reported that sex hormones such as testosterone propionate, androsterone and dehydroandrosterone caused a return of the exophthalmos previously abolished by orchectomy.

I described in an earlier publication (6) the increase in the prominence of the eyes after thyroidectomy in normal guinea pigs. In the preliminary experiments of this investigation, it was found that after thyroidectomy had been performed, preparatory to the administration of thyrotropic hormone, the eyes increased in prominence. That series of observa-

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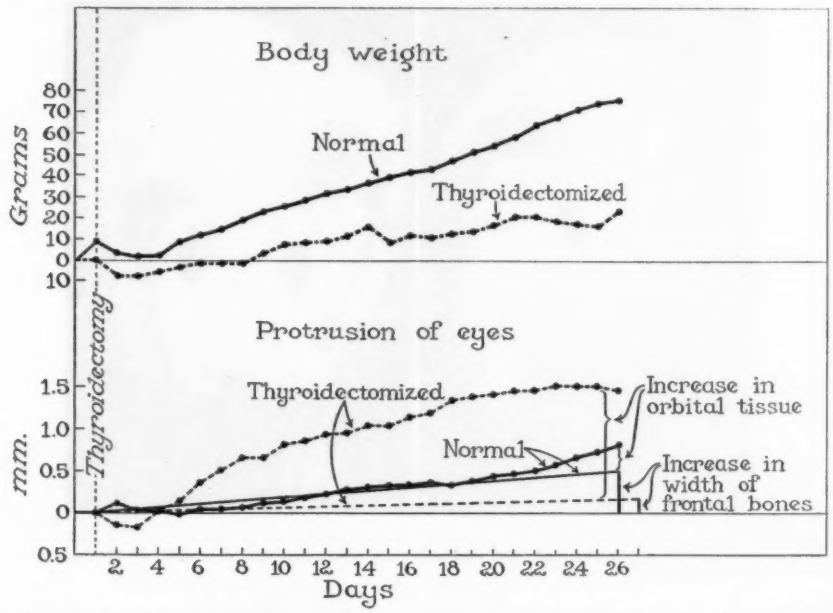


Fig. 1. Changes of the prominence of the eyes resulting from thyroidectomy in the normal guinea pig. The increase in the width of the frontal bones, as illustrated in the lower right, is represented by the same scale as the measurements dealing with the eyes.

tions on the effects of thyroidectomy alone served as a control for the experiments to be described dealing with the effects of thyrotropic hormone.

The control experiment is very briefly reviewed and illustrated. Seventeen growing male guinea pigs weighing from 322 to 500 grams were used. Thirteen were thyroidectomized and 4 served as controls. The intercorneal distance and body weight of these animals were determined at intervals of from 1 to 3 days for 14 to 26 days. It can be seen in Figure 1 that thyroidectomy alone causes some increases of the prominence of the eyes.

EXPERIMENTAL METHOD

The following anterior pituitary products were used in these experiments: (1) antuitrin T prepared for clinical investigation; (2) purified thyrotropic factor prepared for clinical investigation; (3) a crude thyrotropic preparation from the anterior pituitary of swine prepared especially for this study and known to contain small amounts of other known impurities and (4) the specific metabolic principle of the pituitary, which was prepared according to the specifications of Collip and his coworkers (3-5).

Normal guinea pigs weighing between 300 and 400 grams were selected from our Institute stock colony. Animals showing any spontaneous exophthalmos or retardation of growth were avoided. Since color affords greater facility in obtaining accurate eye measurements (6), animals which possessed a white, cream, or buff color about the eyes and which possessed a darkly pigmented iris were selected for study. The animals were maintained on standard laboratory rations consisting of oats, alfalfa hay, beets, and either lettuce or green grass as the season permitted.

The intercorneal distance was determined three times with each of the two methods at intervals of 1 to 3 days. The average of these 6 determinations represented the status of the eyes for that particular day. Body weight was likewise recorded. The animals were thyroidectomized and, after varying lengths of time,

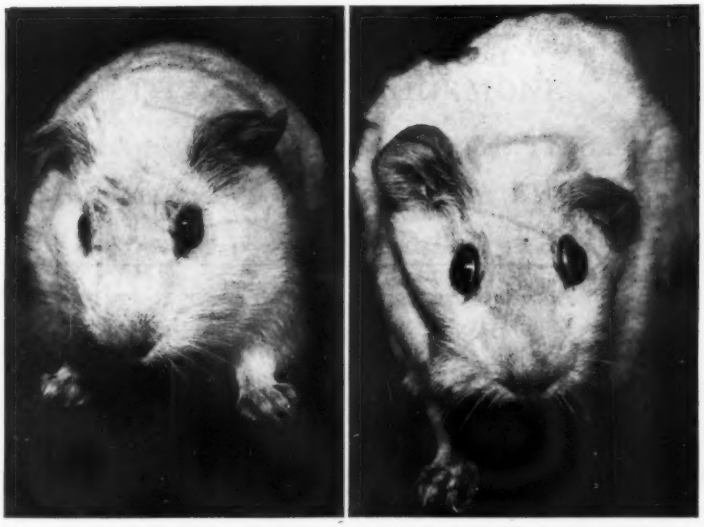


Fig. 2. The gross appearance of exophthalmos produced by antuitrin T (Parke, Davis and Co.). a, left, Normal guinea pig; b, thyroidectomized guinea pig treated with antuitrin T.

were given one of the thyrotropic preparations at daily intervals. Approximately half of the animals in some of the groups observed were not only thyroidectomized but also orchectomized.

At the conclusion of these observations, the animals were killed and the tissues were studied grossly and microscopically with a variety of staining techniques. The results of the tissue observations will form the basis for subsequent reports.

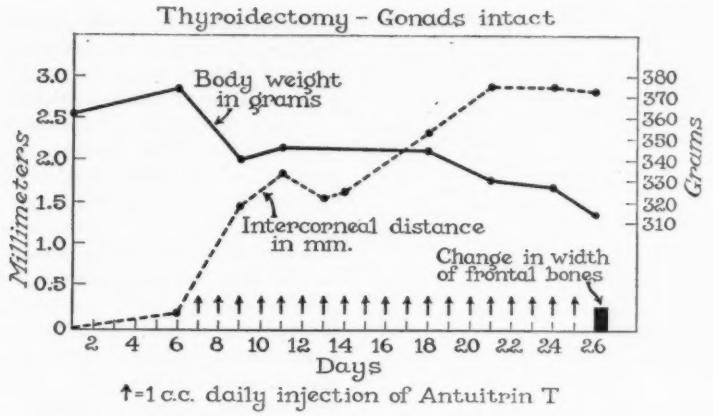
A. THE EFFECT OF ANTUITRIN T ON THE PROMINENCE OF THE EYES IN THE GUINEA PIG

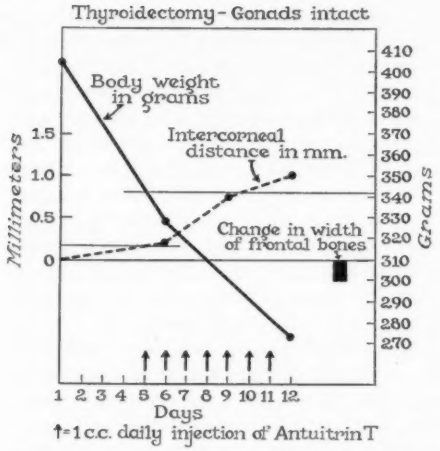
Method. Data assembled from 19 animals comprise the basis of the report on this thyrotropic product. Eight animals were thyroidectomized. Seven were thyroidectomized and orchectomized. Four were normal and served as controls. Five to 11 days were allowed to elapse between the operation and the beginning of administration of antuitrin T, except that in 2 cases, in which the animals were both thyroidectomized and orchectomized, 31 days elapsed before the administration of the hormone was begun. The animals received, by either the intraperitoneal or the subcutaneous route, 0.5 cubic centimeter (1.0 c.c. in 1 case) of antuitrin T containing 25 Junkmann-Schoeller units[1] each day for 3 to 32 days.

Antuitrin T, when given in this amount (0.5 c.c. daily), was found to produce a rather toxic effect on many of the animals. For this reason its administration was on rare occasions discontinued for a day in order to permit the animal to regain its strength.

Because the literature contains controversial opinions concerning the relations of vitamin C to the effects caused by thyrotropic hormone and because these animals were studied during the winter months, when guinea pigs are often on the border line of scurvy, some data were assembled on the effects of giving vitamin C. Accordingly 5 animals were given 2.5 milligrams and 2 were given 5 milligrams of crystalline ascorbic acid daily, intraperitoneally, during the time they received antuitrin T. Ascorbic acid, however, failed to influence in any way the exophthalmos that developed.

[1] That amount of extract which when injected daily for 3 days into guinea pigs weighing 100 to 150 grams causes a recognizable hypertrophy of the epithelium and disappearance of colloid in the thyroid of 2 out of 3 animals (11, 12).





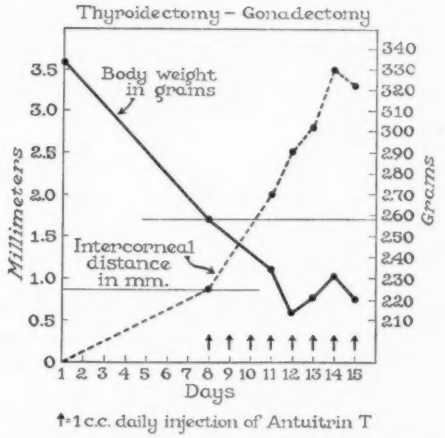


Fig. 3. The changes in body weight and intercorneal distance in animals receiving antuitrin T illustrated by the records of representative animals. Arrows indicate daily injection of antuitrin T. a, above, Thyroidectomy—gonads intact—slight loss of body weight; b, left, below, thyroidectomy—gonads intact—extreme loss of body weight. (Extremes in influence of body weight are shown by a and b. Influence of loss of body weight on intercorneal distance is easily seen. Compare with Fig. 4, showing loss of body weight by fasting.) c, Thyroidectomy and gonadectomy.

Results. Within 30 minutes to 1 hour after the injection of antuitrin T, many of the animals appeared ill. Their state was characterized by inactivity and a ruffled coat. In 12 to 24 hours some animals demonstrated stiffness of the limbs, which in some instances almost amounted to a state of cataplexis.

Definite gross exophthalmos occurred in most of the animals in spite of considerable loss of weight (Fig. 2). The greatest actual increase in intercorneal distance was 3.5 millimeters. Although thyroidectomy *per se* resulted in a protrusion of the eyes, the increase produced by antuitrin T was superimposed in a much more acute and striking fashion. (Compare Fig. 1 with Fig. 3a and c.) With both of the methods of measurement employed there was obtained in most instances an unequivocal increase of intercorneal distance within 24 hours after injection.

The removal of the testes had no inhibitory effect on the development of exophthalmos

TABLE I.—EXOPHTHALMOS OF ANIMALS RECEIVING ANTUITRIN T

	Days of treatment	Weight loss, gm.	Observed exophthalmos, mm.	Correction for weight loss, mm.	Corrected exophthalmos, mm.
Thyroidectomized	3	−50	0.88	+1.00	1.88
	6	−56	0.25	+1.25	1.50
	7*	−77	−0.50	+1.50	1.00
	19	−47	2.50	+0.75	3.25
	7	−132	1.00	+2.00	3.00
	22	−59	2.25	+1.00	3.25
	9	+6	2.75	0	2.75
	7	−100	0.50	+1.75	2.25
Gonadectomized and thyroidectomized	9	−102	3.25	+0.75	4.00
	6	−30	1.63	+0.50	2.13
	32	−14	2.00	+0.25	2.25
	26	−39	1.75	+0.75	2.50
	13	−38	3.50	+0.75	4.25
	16	−30	1.75	+0.50	2.25
	3	−36	−0.25	+0.75	0.50
Intact	12	−47	2.00	+0.75	2.75
	12	−58	0.38	+1.12	1.50
	8†	−134	−0.38	+2.50	2.12
	27	−22	1.50	+0.38	1.88

*Treatment given on 7 of 8 days.
†Treatment given on 8 of 9 days.

(Fig. 3c and Table I). As a matter of fact the two most striking degrees of exophthalmos occurred in animals which had been orchectomized.

Control experiments. It is common knowledge that when an animal loses weight there is a recession of the globes of the eyes into the orbits. Because some of these animals lost rather striking amounts of body weight (Fig. 3b), further observations on the relation of changes in the body weight to changes in the prominence of the eyes were indicated. Furthermore, it was necessary to know whether the solvent in which the active principle of antuitrin T was dissolved or the preservative present in the solution could cause exophthalmos or the toxic effects observed in these animals.

When the solvent,[1] including the preservative but without the pituitary ingredient, was given in comparable amounts to 6 control animals there were no increases in the intercorneal distances nor were there evidences of a toxic influence, such as hitherto observed.

In a second control experiment the changes in the intercorneal distance were studied in animals whose body weights were decreased by fasting. Food was withheld from 5 animals comparable to those used in the preceding experiment but drinking water was provided *ad libitum*. These animals lost from 30 to 40 per cent of their body weight in 10 to 16 days. Their body weights and the changes in their intercorneal distances were recorded at frequent intervals. As the retrobulbar tissue became depleted concurrently with atrophy of comparable tissue elsewhere in the body, the globes of the eyes receded into the orbit. The correlation between the regression in the prominence of the eyes and the decrease in body weight is illustrated by a representative animal of this group (Fig. 4). This illustration shows that for the first 40 grams of loss in body weight in an animal of this size there was a decrease in intercorneal distance equal to the amount *a*. For an additional loss of 40 grams of body weight an added regression equal to the distance *b* resulted and so on.

On the basis of these correlations between decreases in weights of body and regressions of eyes, correction factors have been devised for use in the interpretation of the eye measurements assembled from animals which had been treated with antuitrin T and had lost weight. An animal which lost considerable weight when antuitrin T was administered is illustrated (Fig. 3b). Although the prominence of the eyes in this animal (Fig. 3b) increased relatively little, there was an exophthalmos-producing mechanism which prevented a regression of its eyes such as occurred in the fasting animal which lost a comparable amount of weight (Fig. 4). With the application of the correction factors it has been possible to evaluate the exophthalmos-producing effect of antuitrin T more accurately, thus correcting for the loss of tissue volume in the orbit associated with loss of weight. Table I has been compiled in this way.

It will be seen that 3 of the 19 animals sustained a slight decrease of the prominence of

[1]The information necessary for the preparation of the solvent for antuitrin T was obtained from the manufacturer.

the eyes while receiving antuitrin T. The decrease, however, was not of the magnitude of that sustained by a fasting animal losing the same amount of weight. On the other hand, some animals showed considerable increase in the prominence of the eyes in spite of considerable loss of body weight. After a correction of the exophthalmos based on the loss of body weight, it can be seen (Table I) that the exophthalmos produced in gonadectomized animals was as great as that in animals with testes intact. Except for 2 animals which were orchectomized and in which more striking exophthalmos developed, the 2 groups of animals were essentially equal in this regard.

In the 4 intact animals which received antuitrin T, there did not develop a degree of exophthalmos comparable to that of the thyroidectomized animals even though correction for losses of body weight was made. This difference may be explained at least in part by the data derived from control experiments which illustrated how thyroidectomy alone produced some increase of the prominence of the eyes.

Comment. The importance of accurately correlating changes in body weight with changes in the prominence of the eyes is clearly illustrated. Loeb and Friedman and also Smelser (32, 34) recognized a regression of exophthalmos in animals which lost considerable weight. It is common knowledge that thyroxine, whether of endogenous or of exogenous origin, will cause a loss of body weight. Many authors have reported that exophthalmos was produced less readily in intact animals than in thyroidectomized animals. Absence of the thyroid presumably precludes the possibility of thyrotoxicosis developing when thyrotropic hormone is given. It has been pointed out by Marine (18) in intact animals and Smelser (34) in thyroidectomized animals that thyroxine, when administered to animals simultaneously with thyrotropic hormone, diminishes the exophthalmos. It has also been shown that after the administration of thyrotropic hormone to normal animals for several weeks the incidence of exophthalmos increases considerably. Friedgood (8) has shown that this latent exophthalmos develops later, when the thyroid of the animal has become refractory to the influence of thyrotropic hormone. When this phase is reached the basal metabolic rate falls, evidence of thyrotoxicosis disappears, and the animal usually gains weight. At this time the prominence of the eyes would be expected to increase.

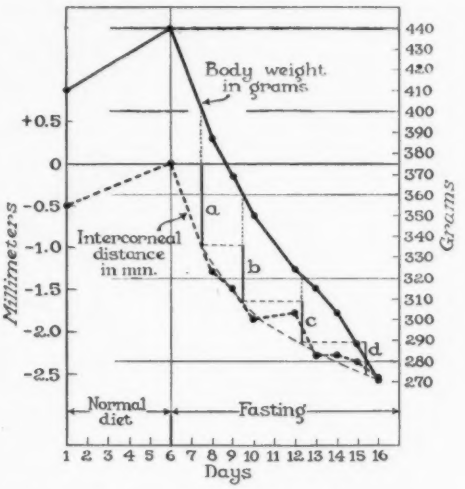


Fig. 4. The changes of body weight and intercorneal distance in a fasted animal. *a*, The decrease in the prominence of the eyes coincident with the first 40 gram loss of body weight. *b*, The decrease in the prominence of the eyes coincident with the second 40 gram loss of body weight. *c*, The decrease in the prominence of the eyes coincident with the third 40 gram loss of body weight. *d*, The decrease in the prominence of the eyes coincident with the fourth 40 gram loss of body weight. (Compare with Fig. 3a, b, and c.)

These experiments reported here which correlate fluctuation of body weight with changes in the prominence of the eyes contribute to our understanding of some of the differences in interpretation of exophthalmos which have appeared in the literature.

B. THE EFFECT OF A "PURIFIED" THYROTROPIC FACTOR (ARMOUR[1]) ON THE PROMINENCE OF THE EYES IN GUINEA PIGS

Method. This product was administered in 0.5 and in 1 cubic centimeter (in one instance 2 c.c.) daily amounts to 8 male guinea pigs. Six of these animals had been thyroidecto-

[1]Assayed and found to contain 5 Rowlands–Parkes units per cubic centimeter according to the manufacturer. One Rowlands-Parkes unit is that amount which when injected daily for 5 days into a 200 gram female guinea pig will cause the thyroid to double its weight or attain a weight of 60 milligrams (28).

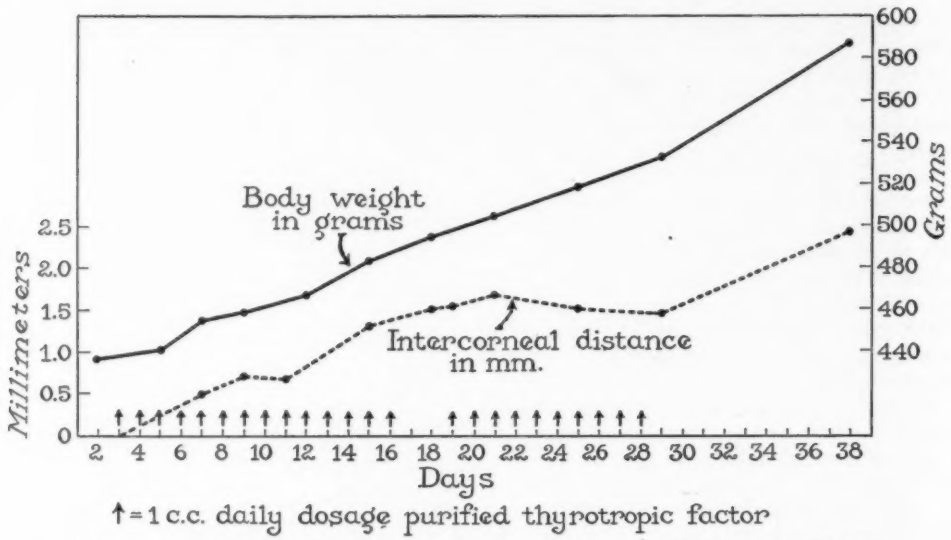


Fig. 5. Changes of intercorneal distance and body weight in a thyroidectomized guinea pig receiving purified thyrotropic hormone. The increase of intercorneal distance is comparable to the increase caused by thyroidectomy alone. (Compare with Fig. 1.)

mized. One of these had also been orchectomized. Two others were subtotally thyroidectomized. The administration of this so called purified thyrotropic factor was begun 2 to 4 days after thyroidectomy, except for one animal, which began to receive 2 cubic centimeters of the preparation on the 16th post-operative day. All animals received the product for periods ranging from 7 to 39 days.

TABLE II.—CHANGES IN THE PROMINENCE OF THE EYES INDUCED BY PURIFIED THYROTROPIC HORMONE

Operation	Treatment		Increase of intercorneal distance, mm.	Change of body weight, gm.
	Days	Amount, c.c.		
T*	35	1.00	1.50	+93
T	39	0.50	2.50	+72
T	34	1.00	2.50	+8
T+G*	21	0.50	0.38	+82
T	14†	0.50	1.63	−27
Subt. T*	36	0.50	1.75	+183
Subt. T	33	0.50	2.00	+65
T	7	2.00	0.75	+40

*T = thyroidectomy; T + G = thyroidectomy and gonadectomy; Subt. T = subtotal thyroidectomy.
†Treatment given on 14 of 16 days.

Results. In contrast to antuitrin T, this "purified" thyrotropic product in the amount given did not cause a loss of body weight nor did it cause the toxic manifestations previously described. Furthermore it did not produce very definite evidence of exophthalmos (Fig. 5). It would appear that the increase of the prominence of the eyes in these animals occurred in a manner comparable to that seen in growing animals which had been thyroidectomized alone (compare Fig. 1 and Fig. 5). In view of the weight which was gained, the increase of intercorneal distance certainly is not striking (Table II). Two animals, however, obtained an increase which was out of proportion to the changes in body weight. Demonstrable differences in the effects due to the different doses administered were not evident, for one animal which received 2 cubic centimeters (containing 10 Rowlands–Parkes units) daily described no appreciable change in the intercorneal distance, further evidence that this pituitary-thyrotropic preparation in the amounts given had relatively little or no exophthalmos-producing effect.

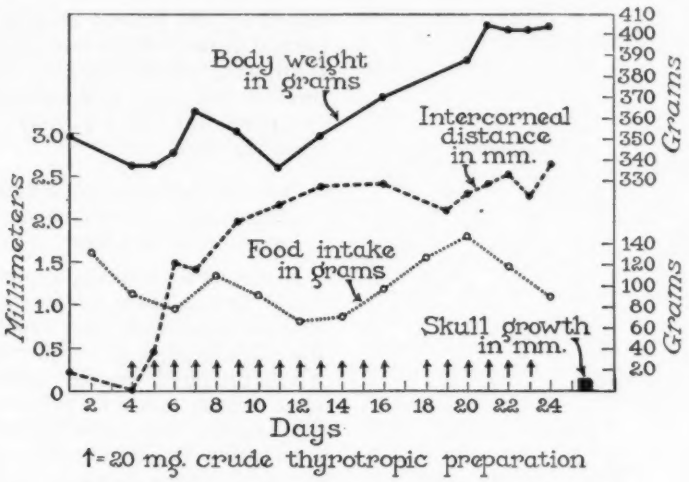


Fig. 6. Changes of intercorneal distance, body weight and food consumption in a thyroidectomized animal receiving crude pituitary thyrotropic factor. Thyroidectomy was performed 3 days before administration of the crude thyrotropic preparation was begun. Arrows indicate injection of 20 milligrams of the product.

C. THE EFFECT OF A CRUDE PITUITARY THYROTROPIC PREPARATION[1] ON THE PROMINENCE OF THE EYES IN GUINEA PIGS

Because the "purified" thyrotropic factor caused hyperplasia of the epithelium of the thyroid but did not induce appreciable exophthalmos, the question arose whether, in the process of "purification," the product may have lost its exophthalmos-producing quality. Some investigators have suggested the possibility that the anterior pituitary may contain two factors, one of which causes exophthalmos and the other thyroid hyperplasia.

A crude thyrotropic preparation was made from the anterior pituitaries of swine in a manner comparable to that employed in preparing the "purified" thyrotropic factor, except for the efforts at purification. This product was reported by the manufacturer to contain some adrenotropic and some gonadotropic principles in very minute quantities.

Method. Ten animals were used in this study. Six of the 10 animals were thyroidectomized and 4 were thyroidectomized and orchectomized. Three to 10 days after thyroidectomy, daily administration of 20 milligrams of the powdered crude thyrotropic preparation, suspended in water, was begun. After 6 days of this administration, the amount was increased to 40 milligrams in half of the animals. This however, caused very little if any added effect on the exophthalmos that already had been produced by the smaller amount.

Before this crude thyrotropic product was given, 2 of the animals received each day for 5 days, 1 cubic centimeter of the so called purified thyrotropic factor, bearing the same lot number as that used in the preceding experiment. Since these injections proved ineffective in producing exophthalmos, the administration of the crude preparation in the same unit dose was begun. The changes in body weights and in intercorneal distances were observed at frequent intervals as previously described. In addition the consumption of food was carefully determined.

Results. On administration of this crude thyrotropic preparation the animals were less lively than normal but there was no profound change in the animals' appearance or in their

[1]Kindly prepared by the manufacturer for this experiment under the direction of Dr. F. Fenger, and assayed and found to contain 5 Rowlands-Parkes units per 4 milligrams of powdered extract. See preceding footnote for definition of unit.

TABLE III.—CHANGES OF INTERCORNEAL DISTANCE AND BODY WEIGHT OF ALL ANIMALS RECEIVING THE CRUDE THYROTROPIC PREPARATION

Daily dose	Operation	Days of treatment	Change of body weight, gm.	Observed exophthalmos, mm.	Corrected exophthalmos, mm.
20 mg.	T*	21	+53	2.50	2.50
	T	12	+24	2.25	2.25
	T+G†	12	+10	2.25	2.25
	T	8	+15	2.00	2.00
	T+G	8	−20	1.50	2.00
20 mg. for 6 days followed by 40 mg.	T	11	+4	1.00	1.00
	T	24	+125	2.13‡	2.13
	T	24	+124	3.50‡	3.50
	T+G	18	−8	1.00	1.00
	T+G	10	−46	0.75	1.25

*Thyroidectomy.
†Thyroidectomy and gonadectomy.
‡The width of the frontal bones increased 0.5 mm. in each of these animals, an observation which explains in part the increase of exophthalmos.

activities such as seen in animals receiving antuitrin T.

The food intake paralleled the changes of body weight (Fig. 6). Instead of losing weight as did the animals receiving antuitrin T, these, for the most part, gained slightly. Two of the animals receiving the product for a longer time than the other animals gained considerable weight. In these 2 instances, the increase in intercorneal distance was due in part to the growth of the skull, for in these 2 animals the width of the frontal bones between the orbits increased 0.5 millimeter.[1]

The exophthalmos produced by the amounts of this crude product given was not as striking as that produced by antuitrin T, although the eye changes were grossly evident (Fig. 6, Table III). Previous orchectomy had no apparent inhibitory effect on the exophthalmos.

Although bio-assays, in Rowlands-Parkes units, of the crude and "purified" products indicated that the amounts of thyroid-stimulating substance given were comparable, yet exophthalmos resulted only in animals which received the crude preparation. The difference in the exophthalmos-producing effect of the "purified" and crude products is further illustrated by the prompt increase in the intercorneal distance of the two animals previously mentioned, which took place when the crude product was given, although the animals had just previously failed to respond to the "purified" product.

[1]The method of control of skull growth is described elsewhere. (6)

D. THE EFFECT OF THE SPECIFIC METABOLIC PRINCIPLE[2] ON THE PROMINENCE OF THE EYES OF GUINEA PIGS

In the two preceding experiments, it was found that a crude product produced both thyroid hyperplasia and exophthalmos. On the other hand, a so called purified product, which produced thyroid hyperplasia to the same degree, failed to induce exophthalmos. The question arises whether in the process of purification an exophthalmos-producing substance may have been lost. This prompted an effort to find a substance which would produce exophthalmos but would not produce thyroid hyperplasia.

Billingsley, O'Donovan and Collip (3) separated a thyrotropic preparation into two fractions. The thyroid-stimulating fraction raised the basal metabolic rate over a period of a number of days by its stimulating effect on the thyroid. The other fraction, known as the specific metabolic principle, caused an elevation of the basal metabolic rate within several hours but did not induce hyperplasia of the thyroid.

Since antuitrin T induced a loss of body weight and a striking exophthalmos while the other products in the amounts given were less effective in these respects, a study of the exophthalmos-producing effect of the specific metabolic principle was undertaken.

Method and results. The specific metabolic principle was administered to 4 thyroidectomized guinea pigs. The previously described methods of observation were used. On the 3rd postoperative day the daily administration of 1 cubic centimeter of this product to 3 animals was begun. After 2 injections had been given and 48 hours had elapsed, there was no definitely demonstrable increase in the intercorneal distance in any of the 3 animals. The daily administration was then increased

[2]This product conformed to the specifications described by its discoverers (3, 4, 5).

to 2 cubic centimeters and the larger amounts also were given to a 4th animal. After 7 to 9 days there was still no evidence of an exophthalmos-producing effect from this product. It was noted that in the 2 animals in which a little more than 1 millimeter increase of intercorneal distance developed, most of this increase occurred after thyroidectomy and before the administration of the specific metabolic principle. Data on this experiment are given in Table IV.

TABLE IV.—CHANGES OF BODY WEIGHT AND INTERCORNEAL DISTANCE IN FOUR THYROIDECTOMIZED GUINEA PIGS RECEIVING SPECIFIC METABOLIC PRINCIPLE

Days of treatment	Change of body weight gm.	Observed increase of exophthalmos, mm.	Corrected increase of exophthalmos, mm.
7	+16	0.25	0.25
7	+33	1.25	1.25
7	+45	1.25	1.25
9	−27	0	0.50

SUMMARY

The exophthalmos-producing effect of several different preparations of thyrotropic hormone has been studied. In addition the effect of the presence or absence of the testes and thyroid on the development of exophthalmos was observed. The gradual changes in the prominence of the eyes of guinea pigs have been observed by two improved methods of measurement which were used at frequent intervals.

It was found that 25 Junkmann-Schoeller units daily of antuitrin T caused toxic manifestations, a loss of weight and a striking degree of exophthalmos in thyroidectomized as well as normal animals. A so called purified thyrotropic preparation, given in quantities of 2.5, 5.0, and 10.0 Rowlands-Parkes units daily, did not produce appreciable exophthalmos nor toxic manifestations in the thyroidectomized animals but did cause hyperplasia of the epithelium of the thyroid in intact animals. A crude thyrotropic product, given in the same concentration in terms of thyroid-stimulating effect as the "purified" preparation, produced exophthalmos and slight toxic manifestations in thyroidectomized animals as well as hyperplasia of the epithelium of the thyroid of intact animals.

In many instances the development of exophthalmos was recognizable within 24 hours after the administration of antuitrin T.

Because loss of body weight is usually associated with a regression of eyes and because many of the animals receiving antuitrin T lost weight, control observations were made on the regression of the prominence of the eyes of animals that were caused to lose weight by fasting. These observations contributed much to the interpretation of changes in the prominence of the eyes of animals that lost comparable amounts of body weight because of the effects of some of the thyrotropic products. A correction for the loss of weight and concurrent change in the eyes in thyrotoxic animals indicated that the exophthalmos-producing quality of thyrotropic hormone was less effective in intact animals than in thyroidectomized animals. This difference was thought to be due to the superimposed exophthalmos-producing effect of thyroidectomy alone (6).

Because the specific metabolic principle raises the basal metabolic rate but fails to stimulate the thyroid and because it is a fraction of thyrotropic hormone preparations, it was investigated for exophthalmos-producing qualities. This principle did not produce exophthalmos.

Approximately half of each group of animals that were studied were orchectomized. It was found that orchectomy had no inhibitory effect on the exophthalmos produced by thyrotropic hormone.

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MASSIVE ISLET CELL TUMOR OF THE PANCREAS WITHOUT HYPOGLYCEMIA

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NEOPLASMS of the pancreatic islet tissue are usually recognized clinically by their ability to produce hypoglycemia with vasomotor and central nervous system manifestations. The islet cell tumor need not be of large size to produce symptoms of hyperinsulinism and indeed it is unusual to find one of considerable bulk that fails to exert an appreciable physiologic effect. The great majority of these tumors are composed histologically of mixed alpha and beta cells or exclusively beta type cells and exhibit distinct secretory granules in their cytoplasms. In most instances the growth is benign. A number of questionable and a few undoubted malignant cases have recently been carefully tabulated and discussed (1, 4).

The case under consideration appears unique in that it concerns a patient harboring a singularly large islet cell pancreatic tumor without clinical or biochemical evidence of hyperinsulinemia. Histological study of the resected tumor showed it to be composed almost exclusively of functionally inactive delta type islet cells. Both the unusual microscopic composition and biologic behavior of this neoplasm appear worth recording.

CASE REPORT

A white female, 40 years of age, was first admitted to the pre-clinic on August 7, 1933, complaining of a periodic gnawing sensation in the epigastrium which appeared 1 to 2 hours after eating and radiated posteriorly to her back. These episodes had been present intermittently over a period of 4 years with symptomless intervals lasting 1 to 2 months. The pain was relieved by taking food and aggravated by fatigue. Her appetite was usually good; apples were recorded as the only food for which she had an idiosyncracy. There was no history of hematemesis, icterus, bloody or tarry stools. Investigation of her past history showed that 5 years previously she had had a uterine suspension and appendectomy performed. Her convalescence was complicated by postoperative pneumonia. There had been no other known illnesses. Her husband had died some time previously and was reported to have had acquired central nervous system syphilis. A son by him exhibited interstitial keratitis. The patient had not received antiluetic therapy and two blood Wassermann reactions taken at this time were recorded as negative.

The patient was an obese, white female, weighing 202.5 pounds, who presented tenderness to palpation in the epigastrium and over both right lower and upper abdominal quadrants. No masses were palpable. Some tenderness was present at the right costovertebral angle at the level of the 11th and 12th dorsal vertebrae. A roentgenologic study of the gastroenteric tract August 8, 1933, showed the stomach to be of the high transverse type exhibiting hypertonicity and hypermotility. No mucosal defects were demonstrable in the stomach or duodenum. Gastric analysis (Ewald test meal) showed a free hydrochloric acid content of 74 degrees and a total acidity of 90 degrees. She was placed on a limited diet with alkali administration which relieved her pain and produced general subjective improvement. She was observed at intervals in the out patient department until 1935 when it became impossible to continue her visits as she now was unable to take leave from her job to attend the clinic. She stated that she felt well except when she neglected to take the alkaline powders. She was not seen again until April 11, 1938, when she visited the gastric clinic after an absence of about 3 years. She stated that she had been well and free of symptoms until September, 1937, when her previous complaints returned and became progressively more severe. She was forced to remain in bed during the month of February. Once during this period she suffered an attack of vomiting, which culminated in a severe gastric hemorrhage and she was brought to a hospital and placed under observation for 1 week. Improvement under treatment was rapid though she continued to complain of a burning sensation in the epigastrium. She was advised to continue on a Sippy diet. Her weight was now 165 pounds. There was moderate tenderness to palpation in the right upper quadrant and pain was elicited over the descending colon. A firm mass having a sharp irregular edge was palpated below the costal margin in the left upper part of the abdomen. This was tender to pressure and was thought to be the spleen. Roentgenologic study performed on April 18, 1938, and repeated on May 3, 1938, showed the duodenal cap to be definitely deformed and irritable with extremely marked

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localized tenderness present. A diagnosis of acute duodenal ulcer was made. A blood Kahn test performed May 10, 1939, was negative. The red blood cell count was 3,800,000 and the white blood cell count 5,000. Considering that the palpable mass in the left upper abdominal quadrant might represent a misplaced kidney, the patient was admitted to the hospital on the genitourinary service. Flat plates of the abdomen and bilateral retrograde pyelograms failed to reveal any renal abnormalities. She was discharged to the gastric clinic for further observation. On June 2, 1938, a barium enema showed the palpable mass in the left upper abdominal quadrant to be medial to the descending colon and at the level of the lower pole of the left kidney. The colon was not displaced in this region. A gastroenteric series on July 19 showed no essential changes in the duodenum from the previous examination and the patient seemed improved on the prescribed ulcer therapy. On May 15, 1939, she again returned complaining of having vomited intermittently during the preceding 5 weeks and of being unable to retain any food during the past week. She was admitted to the hospital feeling very weak and continuing to suffer from abdominal pain and repeated vomiting. The red cell count was 4,170,000 and the white blood cell count 8,500. The mass noted in the left upper abdominal quadrant remained unchanged to palpation and no new light was shed on its nature. She again responded well to medical treatment for her duodenal ulcer and was discharged as improved 1 month after admission and advised to continue on a Sippy diet. A return of her ulcer symptoms sufficiently severe to require hospitalization occurred again on October 25, 1940. Physical examination was essentially unchanged from the last hospital examination. The roentgenologist now demonstrated the presence of a diverticulum of the proximal part of the second portion of the duodenum with irritability of the entire first and second portions and suggested that the mass might be in the pancreas. A spinal fluid Wassermann and gold curve were recorded as negative on December 12, 1940. The patient was discharged on January 11, 1941, with a clinical diagnosis of diverticulitis of the duodenum with probable ulcer formation. She was placed on Sippy powder and atropine. She was instructed to return to the gastric clinic. On January 29, 1941, she was readmitted with the familiar story of epigastric pain and vomiting. A severe attack of hematemesis had occurred 2 days prior to admission. Physical examination showed that the abdominal mass in the left upper quadrant first detected 3 years previously was little changed. Diffuse epigastric tenderness was present but no other pertinent findings were present. A blood pressure reading was 132/84. The red blood cell count was 3,760,000 and a white blood cell count 12,700. Examination of a stool specimen for occult blood gave a slightly positive reaction to the guaiac test. A diagnosis of penetrating duodenal ulcer was made and gastric resection was believed to offer the best hope for lasting relief of her symptoms. The upper left quadrant abdominal mass was thought to represent matted loops of adherent intestines and omentum, the result of leakage from the ulcer crater. The possibility of a retroperitoneal neoplasm of undetermined type was also considered.

On February 26, 1941, an exploratory laparotomy was performed. The scar of a duodenal ulcer could be seen and felt, but there was no crater present and no signs of activity. On exploring the left upper abdominal quadrant a circumscribed hard nodular mass was made out in the region of the body and tail of the pancreas. Closer inspection showed it to have apparently replaced most of this organ and to be adherent to the jejunum, stomach, and spleen. It was firm, well encapsulated, larger than a fist, and fairly freely movable. No metastases could be made out. The mass was exposed through the gastrocolic ligament, carefully dissected free, and removed *in toto*. A large vein penetrating the tumor was thought to be occluded by tumor tissue; this was stripped of its contents and ligated. The patient exhibited symptoms of shock 12 hours after operation but responded well to supportive measures and thereafter made an uneventful recovery. Gross examination of the excised tumor mass showed that the specimen consisted of a well encapsulated round nodular grayish-white mass 12 by 8 by 6 centimeters in diameter. Firmly adherent to one portion of its surface and blending intimately with the substance of the tumor was a flattened well lobulated portion of pancreatic tissue about 2 by 1 centimeter in diameter. Elsewhere small tabs of adipose tissue were adherent to the tumor surface. The cut surface of the tumor was uniformly dark reddish-gray; one small subcapsular area appeared yellowish and soft as though necrotic. Several small portions were removed from the surface of the tumor for microscopic examination. The remaining large mass was sectioned across its greatest axis into two equal halves; one of these was prepared for paraffin embedding *en bloc*, the other used for further sectioning and study with different stains. The generous size of the tumor, even if allowance is made for previous trimming and shrinkage following fixation, can be appreciated (Fig. 1).

Microscopic examination of sections taken from the attached portion of the pancreatic tail showed some hypertrophy of the islets of Langerhans in the still undamaged acinar tissue. The cells composing the islets possessed a rather abundant clear cytoplasm enveloping their uniform round central nuclei. This cell type bore a striking resemblance to small compact round areas of tumor infiltrating the tissue within the acinar portion of the gland (Fig. 2). The cell nuclei of the tumor cells however were larger, the chromatin sparse and irregularly disposed in small threads. No nucleoli were present. With ordinary stains the appearance of the nuclei was unlike that of alpha or beta type cells. The tumor cells ranged from about 15 to 20 micra in diameter with the nuclei composing slightly more than one-

half of the cell diameter. Special stains for cytoplasmic detail, by means of both the Mallory-Azan and the Gomori techniques, failed to reveal the presence of alpha or beta cell granules. Sections taken from numerous widely separated portions of the tumor showed a strikingly uniform cell type and arrangement resembling the delta cell of pancreatic islet tissue. In most instances the tumor was composed of broad sheets, divided by elongated connective tissue trabeculae of varying thickness (Fig. 3). Some zones were completely walled off into circular nests of round and oval cells. In a rare zone the cells became more columnar resembling duct epithelium. The cytoplasm of the cells in the larger zones stained light pink with eosin, with an occasional one showing a clear zone about the nucleus. All portions of the tumor possessed a rich vascular supply. About some capillaries the cells assumed a rosette pattern. In a few areas small clumps of cells were found lodged within the lumina of the vascular channels. No portion of the tumor showed any striking variation in cell size or shape. Mitotic figures were present but not numerous. The thin capsule surrounding the tumor was invaded by nests of uniform tumor cells at many points and these cells also penetrated adherent tags of adipose tissue. One attached small pericapsular lymph node embedded with the adjacent fat was almost entirely replaced by tumor.

On account of the finding at operation of tumor in the lumen of a large vein she was given postoperative deep x-ray therapy, and received 10,400 roentgen units between March 17 and April 25, 1941. For several months she complained of some pain in the region of the incision, but this gradually disappeared, and at her last examination at the clinic on February 20, 1942, she was remarkably free of any symptoms. Roentgenologic examination December 17, 1941, still showed deformity of the duodenal cap and the presence of a diverticulum of the second portion of the duodenum.

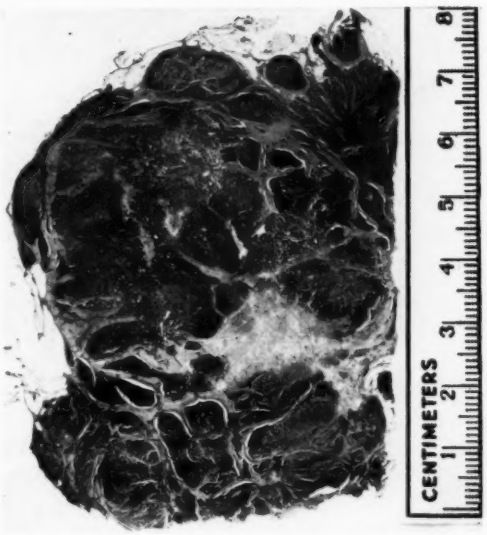

Fig. 1. Cross section of original tumor after fixation and staining.

The patient was seen again May 15, 1943, by request. She had remained free from any digestive disturbances. Her appetite was good and she had regained her usual weight, weighing 210 pounds. She said that recently there had been some discomfort in the abdomen, to the left of and just above the umbilicus. On examination, the incision was well healed, but an indefinite mass could be felt in about the position occupied by the original tumor. This mass was difficult to outline because of her obesity, but apparently did not descend with res-

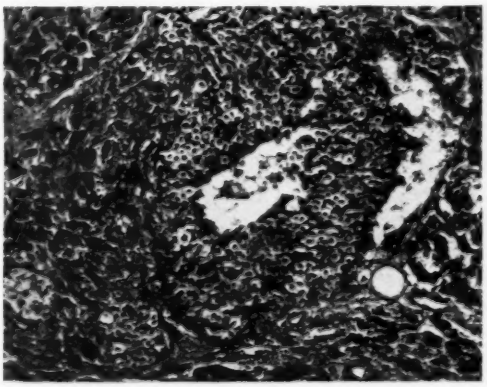

Fig. 2. Portion of tail of pancreas infiltrated by tumor cells bearing a resemblance to islet tissue.

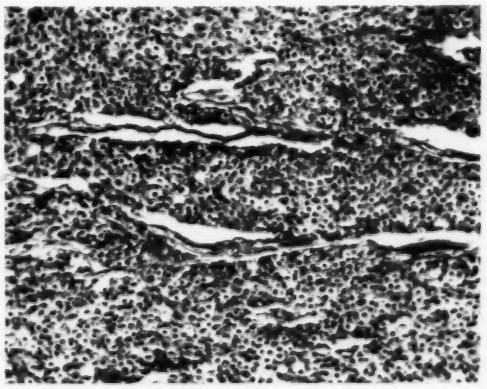

Fig. 3. Broad sheets of uniform appearing cell types composing the bulk of the tumor.

piration. The liver was not enlarged and the spleen could not be felt. X-ray films of the gastroenteric tract showed the stomach to be of the transverse type. There was slight deformity of the duodenal bulb. The second and third portions of the duodenum appeared normal. The palpable mass lay below the stomach, but did not displace it. The colon was negative roentgenologically and its relation to the mass was not determined. The lungs and mediastinal structures appeared normal. Clinically it seemed likely that the tumor had recurred. In the absence of any striking symptoms, she was unwilling to consider any further studies or exploratory operation at this time.

In July, 1943, the patient consented to enter the hospital for a glucose tolerance test which was essentially normal:

	Milligrams per cent
Fasting	98
1 hour	126
2 hours	116
3 hours	93
4 hours	82

About 1 year later, July 13, 1944, she entered the hospital complaining of headache of several months' duration and vomiting of 4 weeks. She also had attacks of dizziness. She said she had lost about 20 pounds in weight though she still weighed 192 pounds. The liver was found to be moderately enlarged with a nodular edge, and a mass on the left side about the size of a fist was found. A glucose tolerance test again showed an essentially normal curve as follows:

	Milligrams per cent
Fasting	97
1 hour	157
2 hours	163
3 hours	132
4 hours	95

A blood sugar determination made from blood taken during one of her dizzy spells was 83 milligrams per cent.

On August 3, 1944, a laparotomy was performed and disclosed a recurrent tumor involving the pancreas, numerous nodules in the liver, and several in the mesentery and omentum. One nodule about 2 to 3 centimeters in diameter in the omentum was removed. Microscopic examination showed an appearance exactly like that of the original tumor.

The patient was discharged from the hospital September 2, 1944, apparently improved. She had minor attacks of abdominal pain and occasional vomiting, for which she was given fairly large doses of tincture of opium. On November 9, 1944, she was suddenly seized by intense epigastric pain, and vomited coffee-ground material. She was admitted to the hospital and although it seemed obvious that she had had a severe intra-abdominal accident, she was treated by nonoperative measures in view of the known extensive malignant disease. Continuous gastric suction and large doses of opiates gave her considerable symptomatic relief, but the temperature and pulse rose and she died November 10, 1944.

Autopsy was performed 3 hours post mortem, the following being an abstract of the pathologic report.

Anatomical diagnoses were: (1) mesenteric thrombosis with infarction of jejunum and hemorrhagic ascites; (2) recurrent carcinoma of pancreas with metastasis to liver, urinary bladder, uterus, and mesentery; (3) duodenal ulcer (chronic).

On opening into the peritoneal cavity 15 cubic centimeters of blood-tinged fluid was found. It was immediately noted that a section of jejunum 50 centimeters in length had a dark purplish-red surface. This extent of bowel was very slightly dilated but no constriction, volvulus, or telescoping was found. The mesentery of this segment of intestine was very dark red and antemortem blood clots were demonstrated in the branches of the mesenteric arteries and veins. The portal vein was occluded by an old blood clot and apparent tumor mass. The head of the pancreas was replaced by a tumor mass 12 centimeters in diameter which projected behind the duodenum and into the lesser curvature of the stomach. The tissue was granular and varied in consistency from mushy to moderately firm. The tail of the pancreas was replaced by another large tumor mass measuring 8 centimeters in diameter. No normal pancreatic tissue was recognizable. The splenic vein was surrounded and occluded by tumor growth. The regional lymph nodes appeared normal. The large liver weighed 2825 grams and had an irregularly roughened external surface due to the projection of nodules varying in size from 1 to 9 centimeters in diameter. These nodules were soft, mushy, and white on the cut surfaces. They were manifestly neoplastic and occupied a considerable proportion of liver volume. The recognizable liver was dark brown, soft, and slightly friable. Part of the portal system was occluded by tumor growth.

Microscopic examination revealed: islet cell carcinoma of the pancreas with massive infiltration of the liver; widespread necrotizing zonal necrosis of the liver, severe hepatitis, organizing pylethrombophlebitis, marked glycogenic infiltration of liver nuclei, marked acute passive congestion of liver; mesenteric venous thrombosis with jejunal infarction and early gangrene, acute mesenteric arteritis, old splenic infarct; chronic interstitial fibrosis of pancreas; organizing thrombus of pulmonary arterioles; mild focal atelectasis and pulmonary emphysema.

The tumor tissue obtained at post mortem looked exactly like the original tumor and the metastatic nodule removed in August, 1944.

SUMMARY

A large tumor of the pancreas was removed from a 48 year old woman who was known to have had a palpable mass in the abdomen for 2 or 3 years, but whose symptoms were

those of duodenal ulcer. Study of the tumor showed it to be an islet cell tumor of the pancreas. Gross findings at operation and microscopic study indicated that it was malignant. At no time were there any symptoms of hypoglycemia and several glucose tolerance tests were normal. Local recurrence and widespread metastases occurred, and the patient died 3 years and 10 months after removal of the tumor, the immediate cause of death being mesenteric thrombosis.

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THE SURGICAL REPAIR OF THE DEEP BRANCH OF THE RADIAL NERVE

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THE injuries to the extremities in war result in large numbers of peripheral nerve injuries. In a 12 months' period 329 explorations of peripheral nerves have been done at this hospital. Of these, 232 were operations for nerve injuries in the upper extremities, 51 were explorations of the radial nerve. In 15 instances the radial nerve has been explored distal to its point of division into the deep (motor) and superficial (sensory) branches.

The injuries to the deep branch of the radial nerve have been due to penetrating wounds of the forearm; extensive soft tissue wounds and fractured bones of the forearm have been the usual associated injuries. The deep (motor) branch of the radial nerve is well protected from pressure, contusion, and superficial injuries. Its injury is rare in civilian life and the characteristic deformity and function loss are most often seen in the regenerating common radial nerve before the regenerating axones have reached the most distal muscles, or those supplied by its deep branch.

It has been regarded that the repair of the radial nerve distal to the point of division into the superficial and deep branches is generally not satisfactory. This was thought to be due to the small caliber of the radial nerve distal to its point of division and because of the difficulty in obtaining sufficient length to close any appreciable defect existing in the continuity of the nerve. Mayfield found these unfavorable factors in the technique of nerve repair could be overcome and usually a satisfactory repair could be accomplished. There are two especially favorable conditions for regeneration in this particular nerve; first, it carries only motor fibers and, second, only a short distance must be bridged before the regenerating axones reach their motor end plates.

Interruption of continuity of the radial nerve distal to the origin of the deep and superficial branches is also distal to the site of origin of at least one motor branch to the extensor carpi radialis muscle group. Consequently extension of the hand at the wrist is not lost, though it is impaired. In the position of extension the hand has a characteristic radial deviation due to the loss of function of the extensor carpi ulnaris muscle. Associated with this functional deformity at the wrist is the loss of extension of the metacarpophalangeal joints of the fingers and thumb, the loss of extension of the distal phalanx of the thumb and abduction of the thumb (Fig. 1).

Such a lesion produces a characteristic deformity as well as serious functional loss.

From the Neurosurgical Section, Ashford General Hospital, White Sulphur Springs, West Virginia.

Fig. 1.

Fig. 1. Characteristic deformity associated with deep radial nerve paralysis. Note extension of wrist with radial deviation, loss of extension of all metacarpophalangeal joints and loss of abduction of thumb.

Fig. 2.

Fig. 2. Side view of characteristic deformity. Loss of abduction and extension of thumb obstructs entry of objects into grasp of fingers. Loss of extension of fingers reduces the reach of the grasp and impairs fine movements of fingers.

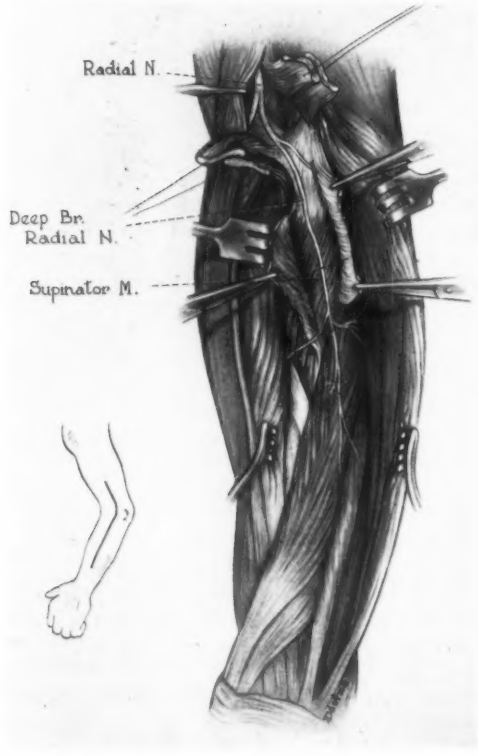

Fig. 3.

Fig. 3. For illustration the extensor carpi radialis muscles have been divided transversely and reflected. The deep branch of the radial nerve spirals posteriorly around the neck of the radius and passes between the superficial and deep planes of the supinator brevis muscle. The extensor carpi radialis brevis and the extensor digitorum communis muscles have been separated to expose the branching of the deep radial nerve as it emerges from the supinator brevis muscle.

Grasping objects is greatly impaired as the dorsum of the thumb impinges on the object. The thumb must first be abducted with the opposite hand in order to encircle the object and oppose the fingers. The fingers cannot be extended to open the hand for grasping; the dorsum of the fingers is slid over a fixed object until the finger tips pass over it and it then comes under the flexion function of the fingers. The loss of fixation of the metacarpophalangeal joints by the extensor tendons results in loss of fine movements of the fingers. Abduction and adduction of the fingers are impossible unless the metacarpophalangeal joints can be extended (Fig. 2). The functional loss resulting from a lesion of this terminal branch is almost as disabling as the loss of the common radial function of the mid arm. Interruption of the continuity of the motor branch of the radial nerve distal to its site of division may result in loss of any one of the functions mentioned, depending upon the nerve branch injured (Fig. 3).

Fig. 4. Dissection of radial nerve showing injury to radial nerve proximal to site of division and site of foreign body in the deep branch. The entire area was resected and a satisfactory end-to-end suture accomplished. *1*, Common radial nerve; *2*, scar between common radial nerve and superficial and deep radial nerves; *3*, deep branch of radial nerve; *4*, superficial branch of radial nerve.

Fig. 5. Findings at operation of patient shown in Figure 3. There is scarring of the deep branch of the radial at its site of division. The extensor carpi radialis and the extensor communis digitorum muscle group have been separated. The vein retractor is holding back the cut superficial portion of the supinator, the branches labeled show the muscles supplied. A branch arising below the supinator muscle to the extensor carpi radialis longus muscle is commonly demonstrated by electrical stimulation though not generally described in the anatomical texts. *1*, Deep branch of radial nerve; *2*, nerve to extensor carpi radialis muscle group; *3*, nerve to extensor communis digitorum muscle; *4*, nerve to extensor carpi radialis brevis muscle; *5*, nerve to extensor carpi ulnaris and extensor digiti minimi muscles; *6*, nerve to abductor pollicis longus and brevis muscles.

The anatomy of the nerve can be described by the surgical approach. An incision is made on the anterolateral aspect of the lower third of the arm, lateral to the elbow joint. It is continued on the dorsum of the forearm to the junction of the middle and lower thirds of the forearm in the palpable groove between the extensor carpi radialis muscle group and the extensor digitorum communis muscle. Such an incision passes posterior to the lateral cutaneous and anterior to the posterior cutaneous nerve of the forearm and does not cross the flexion crease of the elbow. It allows the anterior border of brachioradialis muscle in arm and forearm and line of cleavage between extensor communis digitorum and extensor carpi radialis muscles to be easily explored.

The cleavage line between brachioradialis and brachialis muscles is then developed and as the brachioradialis muscle is retracted lat-

Fig. 6. End-result in Case 1. Note tendons of extensors and abductor of thumb. There is residual weakness of the extensor of the middle finger.

Fig. 7. Result in Case 3. Note loss of most proximal portion of substance of extensor muscles from initial débridement of wound. The residual muscles provide satisfactory extension and abduction of the digits following nerve regeneration.

erally the common radial nerve is exposed. Branches to the brachioradialis and extensor carpi radialis longus muscles emerge from the lateral side of the nerve. The medial side is safe for dissection.

The radial nerve usually divides into the superficial and deep branches at about the level of the elbow joint (Fig. 4). The more medial or superficial branch of the nerve can be traced downward into the forearm beneath the brachioradialis muscle. It becomes subcutaneous in the distal third of the forearm. This is a purely sensory nerve and its injury is of minor importance when compared to the injury of its motor division.

The second terminal branch of the radial nerve is ordinarily known as the posterior interosseous branch, the deep branch, or the motor branch. This nerve passes anterior to the capsule of the elbow joint, then continues laterally and posteriorly to curve about the neck of the radius beneath the superficial portion of the supinator muscle. A motor nerve branch to the supinator muscle is usually given off the lateral side of the deep radial nerve a short distance above its passage into the supinator muscle.

To expose the nerve distal to the supinator muscle, the dissection is made on the dorsum of the forearm. There is a palpable groove between the extensor carpi radialis and the extensor digitorum communis muscles in the middle third of the forearm and dissection will develop this line proximalward along the intermuscular septum from which some of the muscle fibers of both groups of muscles originate. When the extensor carpi radialis muscles are retracted laterally and the extensor communis digitorum muscle is retracted medially the deep branch of the radial nerve will be exposed at its point of emergence from the supinator muscle. Medial branches to the extensor communis digitorum and additional lateral branches to the extensor carpi radialis muscles are given off only a short distance from its site of emergence from the

Fig. 8. Result in Case 4. Near complete abduction of thumb and extension of the digits has been regained.

Fig. 9. Extension of wrist and digits obtained by tendon transplantation when radial nerve was irreparable.

TABLE I

Case No.	Date	Injury in relation to supinator muscle	Defect in cm.	Operative procedure	Result
1	6-20-44	Distal	4	Repair	Return of function Fig. 6
2	7-19-44	Distal	5	Unsatisfactory repair	Lost to follow-up
3	9-11-44	Distal	2	Repair	Return of function Fig. 7
4	9-29-44	Proximal	4-5	Repair	Return of function Fig. 8
5	10-12-44	Distal	0	Neurolysis	Lost to follow-up
6	2-15-45	Proximal and within	10	Irreparable	Tendon transplant
7	2-23-45	Within and distal	8	Irreparable	Tendon transplant
8	3-23-45	Within and distal	9	Irreparable	Tendon transplant
9	4- 2-45	Within	4	Repair	Too recent for evaluation
10	4- 2-45	Proximal	7	Repair	Too recent for evaluation
11	4- 5-45	Distal	0	Neurolysis	Too recent for evaluation
12	4- 6-45	Proximal	7	Repair	Too recent for evaluation
13	4-10-45	Distal	0	Neurolysis	Return of function
14	4-18-45	Distal	4	Repair	Too recent for evaluation
15	4-23-45	Within	4	Repair	Too recent for evaluation

supinator muscle. The nerve then becomes much smaller in caliber and may give off additional medial and lateral branches but the main trunk continues distalward to reach the extensor pollicis longus and brevis and the abductor pollicis longus muscles. These are terminal branches of the nerve (Fig. 5).

In the surgical exposure of the deep branch it will probably be necessary to incise the superficial portion of the supinator muscle in order to obtain complete visualization and gain length to obtain an approximation if a segment of the nerve has been destroyed. Transplanting the nerve superficial to the supinator and elevation of the common radial to a more superficial position beneath the brachioradialis and flexion of the elbow with the nerve transplanted more superficially permits large gaps to be sutured without tension. An accurate approximation of only the epineural sheath with fine suture material without tension is the essential requisite for nerve suture. The minimum of foreign body and trauma at the line of suture insures minimal inflammatory reaction and fibrosis. If the nerve is injured at the site of its branching, the distal filaments should be approximated by fine sutures through the sheath in order to form a single distal trunk. A more satisfactory end-to-end suture can be obtained in this way than in trying to suture each branch to the single proximal trunk. Following suture of the nerve the elbow is immobilized in a position of flexion for a period of 4 weeks and then gradual extension is permitted to take place.

To close a defect by stretching the nerve either at the time of operation or postoperatively results only in fibrosis of the stretched section and prevention of regeneration. It will be impossible to repair some defects even after an extensive mobilization and transplantation of the nerve to a more superficial position. In these patients tendon transplant will have to be resorted to. The defects in the deep radial nerve in this group of patients are listed in Table I. In the 15 patients in which the deep radial nerve was explored, it has been possible to obtain a satisfactory end-to-end suture in 8. In 3 of these sufficient time has elapsed to expect regeneration and all 3 have shown excellent return of function (Figs. 6, 7, and 8). Four have been regarded as technically irreparable due to extensive loss of nerve tissue. Of these, 3 have been referred to the orthopedic section for tendon transplants (Fig. 9). A neurolysis has been done in 3 patients. In these continuity of the nerve was intact. Two of this group have had return of nerve function since the neurolysis was done.

SUMMARY

The results to date in 15 cases of exploration of the deep or motor branch of the radial nerve are given.

The deep or motor branch of the radial nerve should regenerate well because of its purely motor character and the short distance regenerating axones must span before reaching their motor end plates.

The characteristic deformity and function loss is described and the surgical anatomy discussed. By sufficient mobilization and transplantation of the nerve, moderate defects in the continuity of the nerve may be closed and satisfactory repair may be accomplished.

The early results have been sufficiently good to warrant exploration of injuries to the terminal motor portion of the radial nerve with an attempt to restore its continuity. If destruction of the nerve is of such extent that repair is impossible, tendon transplant, to obtain extension of the digits and abduction of the thumb, should be done.

Additional data have been obtained since this paper was submitted for publication. Twenty-four explorations of the deep branch of the radial nerve have been done. In 4 instances, as listed in Table I, the nerve was irreparable. Suture of the nerve was required in 13 patients. Of these, 9 have shown return of function, 2 are showing beginning return of function, and 2 have shown no evidence of regeneration. Lysis of the nerve was done in 7 patients. All have shown return of function.

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THE TREATMENT OF BURNS

Report of 155 Cases

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THIS series of burns includes 155 patients admitted and treated during 1 year. There were 97 admitted from forward hospitals where the primary dressing was done and 58 admitted directly from the scene of accident with first aid but without initial definitive care. Twenty-six cases, or 17 per cent of the entire series, were third degree burns, the percentage being about the same in the two groups.

This discussion will concern itself almost entirely with the treatment of third degree burns with a description of the methods used and with emphasis on strict adherence to established surgical principles. Not much attention has been paid to the type of emollient used for primary dressings because throughout the series it has been observed that other factors seemed more important. In the group of patients admitted from forward hospitals, a wide variety of materials was used; in the group admitted here, directly from the scene of accident, all were treated identically, and the results were similar in the two groups. It was felt, therefore, that factors other than the emollient were the ones to consider as important. Gradually throughout the series, an attempt was made to improve technique and shorten the time required to get complete skin coverage. By the end of the series, we were accomplishing our aim of obtaining complete skin coverage of third degree burns within 4 weeks of the date of injury.

CLASSIFICATION

Before discussing treatment it is important to establish the method by which a first, second, or third degree burn was diagnosed. When erythema only was noted, the diagnosis was first degree. When erythema plus blisters appeared, the tissue under the blister was inspected as well as could be done without disturbing the blister. When the base of the blister revealed the dermis to be pink and covered with a network of fine blood vessels appearing as multiple red dots, a diagnosis of second degree burn was made. However, when the dermis under the blister was sallow in appearance, or there were only a few visible vessels, a diagnosis of third degree burn was made. Naturally if the destruction went beyond the blister stage to charring, the diagnosis was obviously third degree. In all patients admitted from forward hospitals, the diagnosis made at the forward hospital was accepted and recorded. In only 1 instance was it necessary to change the diagnosis, this injury being a phosphorus burn which was originally called second degree but which eventually required grafting of skin. Certainly infection in the management of these patients did not make third degree burn wounds out of those that should have healed without operative repair.

From a hospital in the Communications Zone.

INITIAL TREATMENT

All cases of the two groups had the following treatment: (1) prompt attention; (2) plasma, 50 cubic centimeters for each 1 per cent of body surface burned, given during the first 24 hours; (3) morphine for comfort; (4) thick pressure dressing with fine mesh gauze next to the burn over a nonirritating emollient; (5) immobilization by the use of pressure dressings with stockinette or elastic pressure; (6) warmth and rest; (7) no change of primary dressing for 7 to 10 days.

All patients from forward installations arrived here in about 4 to 6 days in excellent condition, taking a full diet. In a few, the dressings needed to be reinforced because of shifting in transportation, but most of them required no immediate care.

All of the 58 patients admitted directly to the hospital from the scene of the accident had identical care. They were taken from re-

ceiving to the operating room where all the personnel were required to wear masks and where sterile technique was followed. None of them was anesthetized, none was débrided. Blisters were not disturbed. When mud or dirt from the street had soiled the burned surface it was washed gently with a warm mild soap solution. When no obvious surface contamination was present, no cleansing was done. Some were brought in with a thin dressing over the wound, a few had had a topical application of an ointment. These dressings were removed but no effort was made to remove any medication. Morphine in the meantime was given to those who had none before admission and plasma was started at once by the operating room personnel. As rapidly as possible, sulfadiazine cream in fine mesh gauze strips, which is kept available for that purpose, was laid smoothly over the burned surface. Gauze pads, followed by full thickness cellucotton absorbent pads, were applied, then sheet wadding and plaster of paris for extremities, in order to get maximum immobilization. A section of stockinette was used over the heavy pads for the face and head with holes cut for eyes, nose, and mouth. Over the trunk, the padding was supported by ace bandage.

Even in the extensive burns, the dressing was completed by the time 1 unit of plasma had been given, so the patient, having been kept warm in the meantime, was taken to the ward and put to bed. A note indicating how much plasma he was to receive accompanied the patient to his ward. This amount was calculated rapidly on the basis of 1 unit for each 5 per cent of body surface and usually the entire amount was given promptly, without interruption, in order to prevent hemoconcentration and shock. Warm drinks, rest, and quiet were the rule for these patients, and usually in a few hours they were ready to eat. Even though many patients had severe burns, none developed shock, probably because of the prompt administration of a calculated amount of plasma. Within the first 24 hours copper sulfate determinations were done to evaluate the hemoconcentration. Plasma or whole blood was given as indicated. On the seriously or extensively burned patient, this checkup was repeated frequently during his entire stay in the hospital and blood or plasma supplied whenever indicated. After the initial amount had been given, very few patients required additional plasma. Whole blood, however, was used in the later treatment of 9 patients and will be discussed later.

Of the 129 first and second degree burns, all returned to duty. They had an average of 8 per cent body surface burned and were in the hospital an average of 28 days. No complications developed in this group and none required transfusions. All were treated by initial pressure dressings. Some received chemotherapy, others did not, and since the results were good, gradually less attention was given to chemotherapy in the first and second degree burns. This subject will be discussed in more detail under a separate heading.

LATER TREATMENT

In the first and second degree burns, dressings were changed at approximately 8 to 10 days. These patients were without exception taken to the operating room where sterile technique was the rule. All were premedicated with morphine and atropine, and sodium pentothal anesthesia was used whenever the change of dressing was painful. In approximately half of these cases no subsequent dressing was required. When required, areas were cleansed with warm saline sponge; fine mesh gauze strips, dry or impregnated with sulfadiazine cream, were laid smoothly over the burned surface, and were covered again by padding and pressure immobilization exactly as at the initial dressing. Dressings were changed in the operating room at about weekly intervals until recovery.

In a few cases there was some evidence of exudate and infection but no cultures were made. This infection cleared rapidly and in no instance did it become a cause for a change in the management of the first and second degree burns. All of these soldiers returned to duty in this theater of operations.

The third degree burns cannot be dismissed as simply, and it is with these patients that we were most concerned. Their management required the utmost patience and persistence and after the initial few days had elapsed their treatment was aimed at prevention of infec-

tion, coverage by skin grafting, and supportive measures. It was our observation that the longer skin coverage is delayed, the greater is the problem of infection and supportive therapy. Also the greater the infection, the more difficult the skin coverage. It thus became a race between the surgeon with his skin grafts and the wound with its bacteria.

In this series there were 26 patients with third degree burns, with an average of 20 per cent of body surface involved, all of whom required skin grafts. Two distinct types of pathology were noted in these wounds. Those who had damage, but not destruction, of the full thickness of skin usually had a gradual slough of dermis down to the subcutaneous tissue during the first 2 weeks. Under this slough then appeared the granulating surface. Usually the sloughing was not complete at the first dressing, so the patient was redressed and returned to the operating room in about 4 days. Usually by this time, 2 weeks after the burn, skin replacement was started.

The other type of third degree burn encountered was that in which the entire thickness of skin had been destroyed. By 14 to 21 days, the entire area was well demarcated. It has been our experience that it is best not to wait for this eschar to loosen, and it is a decided mistake to leave it intact until fluid collects under it. As soon as the area of demarcation became evident, the entire eschar was removed by sharp dissection. This procedure was usually carried out about 2 weeks after the burn. Very little bleeding was encountered and secondary hemorrhage was controlled by pressure dressings. In a few days the area was covered by granulation tissue and grafting was started.

On several of our recent patients, we have placed very thin grafts directly on the subcutaneous fat at the time of removal of the destroyed skin without waiting for granulations to form and we have been gratified to see that about 90 per cent of these grafts were successful. In the future we expect to start grafting promptly after removal of the eschar because, from the standpoint of infection, the area is as clean as it ever will be.

It has been our experience that from the time the damaged or destroyed skin is removed, skin replacement must be pushed vigorously until the entire area is covered. Naturally, in extensive burns, it is impossible in most instances to do a complete coverage at one operation. The length of the period of anesthesia and the availability of donor sites limit the amount of work that can be done. No other factor, however, should be permitted to delay the procedure. In some of our early cases we delayed because it was felt that the area was in no condition to receive skin. Always, this was later regretted. It is difficult to improve an area, and the probability of its becoming worse is very real. In a number of instances in which we have grafted areas that were thought to be poor recipient sites, we have lost the grafts, but almost always the area improved sufficiently by the skin dressing so that the next attempt was successful. Skin dressing has been our most successful agent in combating infection with its complications. One of our recent patients with 35 per cent body surface involved had the eschar dissected and removed on the 14th and 18th day after being burned. The grafts were applied the 18th, 22d, and 27th day and the area was completely covered at that time. He may require a few minor plastic procedures in the future, but certainly he has been saved months of disability by prompt and vigorous application of skin.

SKIN GRAFTING

The procedure of skin grafting in the treatment of burns is not the problem of a plastic surgeon. The primary purpose of transplanting skin is to facilitate rapid wound healing in order to preserve the deeper structures involved and maintain the general condition of the patient. Whatever procedures might be necessary later to improve the skin function of the grafted area was not given too much consideration at the time of the original grafting. Whenever possible, thicker and larger grafts were placed in the axilla, popliteal space, and other areas where danger of cicatricial contracture is present, but always, the type of graft that was most certain to grow was used. The healing of the wound and preservation of the muscles, vessels, tendons, and joints were the primary considerations.

Then if the individual could be cured of his burn, remain in good general condition with no loss of function of deeper structures, and be completely covered by good skin instead of tender, adherent, contracting scars, we felt that the treatment of the burn had been adequate. Whatever later skin substitution is necessary, becomes a problem for the plastic surgeon, but, originally, skin coverage was done to save the patient, prevent sepsis, and preserve function. Speed of coverage was the watchword and small thin grafts lent themselves better to this type of surgery than larger and thicker sections.

TECHNIQUE

In an effort to get skin coverage in the shortest possible time, we have tried several methods of grafting. Because of the pressure of work in this theater of operations and since burns seemed to occur when casualties were heaviest, their care coincided with the care of many other injuries. Also with occasional change of personnel, simplification of technique was necessary.

At first we followed the accepted technique of cutting grafts and placing them in saline as they were removed. After all the grafts were cut, they were spread on a moist rubber dam and transferred to the recipient site. This procedure involved unfolding and smoothing out curled edges, as the graft slipped to and fro on the recipient site, and possibly suturing the graft in place. This method was so time consuming and irksome that it was finally discarded.

Next we tried a method which, as far as we have been able to determine, has not been advocated, probably because of the possibility of infecting the donor site. This method is the immediate direct transfer of skin from the donor to the recipient site without passing through saline. We were surprised and pleased with the result. First, it reduces the time required to cover a given area to about one-fourth of the time needed when the section is passed through saline solution and permitted to contract and curl up. Second, the adhesive quality of the freshly cut surface causes it to nestle and cling to its new bed so tenaciously that in a matter of minutes it is almost impossible to disturb it. Sutures are never necessary.

By the direct transfer, particularly of small easily handled sections, the cutting instrument carries the graft to its new site, and a forceps or any available instrument fixes one end of the section. The knife, as it is pulled away smooths the graft over its new home. Even the under sides of suspended extremities can be grafted easily. Graft after graft is laid end to end and side by side, going to and from the donor site so that an entire extremity can be covered in the time ordinarily required to cover the anterior aspect of a leg. The procedure is done easily, rapidly, without annoyance; the grafts adhere well, grow readily, and skin grafting becomes a pleasure. No infection of donor site has occurred.

In recent years, much has been written on the application of adhesive substances to the grafts or recipient site. We have had no experience with the acacia preparation or plasma thrombin or with any other adhesive substance, but believe its use is sound. However, by the immediate direct transfer without washing in saline, we have preserved nature's own adhesive substance to fix the graft to its new location without the use of added adherent.

After the grafts were placed, fine mesh gauze, moist but not wet, was laid evenly over the area. Gauze pads and abdominal pads for gentle pressure were applied. Plaster of Paris casts were put on extremities; ace bandage was used over the trunk, with figure-of-8 for the buttocks and 8 inch stockinette hood for the head and face. Donor sites were sprinkled with sulfanilamide crystals and covered in the same manner as was the grafted area. Four to 6 days later the patient was brought back to the operating room for subsequent grafting of additional areas or a patch here and there where a small area failed to obtain coverage.

Most of our grafts were cut very thin, the average thickness of grafts being less than 0.010 inch. In our experience, generally speaking, the thinner the graft, the better it will grow. Also the recovery of the donor site was much more rapid when thin sections were used. This factor was important in the 11 cases in the series of patients who had over

25 per cent of body surface involved. In these cases it was sometimes necessary to use some of the donor sites more than once. It has been our observation, however, that skin cut from a previously used site does not grow as well; therefore we used a fresh site whenever possible. Most of the donor sites were healed sufficiently to go without dressing in 8 days.

INSTRUMENTS

In an active theater of operations where the patient load at times may become tremendous, the problem of keeping instruments available and in working condition is a very real one. With a large number of burns requiring grafts and several surgeons at work, every instrument that was available, adaptable to skin grafting, and sharp was pressed into service. When the donor sites were adequate, the Padgett dermatome available, and blades sharp, the dermatome was used. However, since sections cut with the dermatome did not lend themselves easily to direct transfer, the Blair knife or a Gillette type razor blade was used more often and the dermatome used only for the coverage of special areas such as axilla or popliteal space. The razor blade, grasped by a curved Kelly forceps, was the ideal instrument when small sections were desired or only a spot here and there needed to be covered. It can be used well by anyone. Those of our group who had never done skin grafting became experts in one easy lesson. By grasping the blade with a curved forceps, held in the right hand while the left hand steadies the field, a strip of skin an inch wide and as long as the donor site will permit can be cut rapidly and easily without assistance. This method lends itself well to the direct transfer of grafts. It has the added advantage of always being available and sharp. A supply of razor blades was kept in sterilizing solution so that the decision of whether or not to graft was never influenced by the availability of sharp instruments.

With rapidly healing donor sites, availability of sharp instruments, and simplicity of method, our group rapidly assumed the attitude that skin is expendable and grafts were placed whenever and wherever possible. In fact, some grafts were placed on recipient sites that looked impossible, frequently with very gratifying results. For example, an area from which a charred eschar was dissected 10 days after being burned had skin placed over a layer of subcutaneous fat that from all appearances was blessed with only a very meager blood supply. Four days later when the dressings were removed, the skin was growing nicely and continued to do well. Areas with granulations so exuberant and vascular that they could not be trimmed down because of bleeding were covered satisfactorily. Areas with soupy exudate were covered by thin sections which grew. In general, our aim was to get skin coverage at the earliest possible moment, and the more vigorously this policy was pursued, the better were our results, both in patient comfort and ultimate function of extremities.

CHEMOTHERAPY

Chemotherapy usually varied directly with the extent and degree of the burn. With first and second degree burns, very little drug of any type was used. Recently these patients have received none and are apparently doing as well as those who received sulfonamides. In the third degree burns, nearly all were given either a sulfonamide or penicillin. In the early cases, when supplies of penicillin were limited, sulfadiazine, 4 to 6 grams daily, was given with frequent checks of blood level. Those patients who showed evidence of sepsis were put on penicillin, 25,000 units every 3 hours. Usually this was continued for about 10 days while skin grafting in stages was continued. One soldier with over 40 per cent of body surface involved had penicillin for 30 days, 200,000 units daily, while skin grafting proceeded. At present we are using penicillin therapy in all extensive third degree burns.

Locally, sulfadiazine cream in fine mesh gauze was used as the initial dressing and was continued on subsequent dressings until it was established whether the burned skin was being saved or lost. On donor sites we sprinkled sulfanilamide crystals and covered these with fine mesh gauze and pressure dressings plus immobilization just as for the burned areas.

A stimulating dose of tetanus toxoid was given to all shortly after the injury.

SEPSIS

If and when infection developed in the open wound of a third degree burn, the problem was a real one. Particularly was this true in the summer when flies abound. Some patients during transportation could not be adequately protected from flies and at the removal of the initial dressing, it was not uncommon to encounter maggots. Once hospitalized at a fixed hospital where the treatment could be carried on without interruption, adequate fly control, rigid use of nets, sprays and screening, when available, soon reduced the flies.

The infection of Bacillus pyocyaneus with its bluish exudate was frequently present. When the exudate was not profuse, it was disregarded and grafting continued. When profuse, openings were put into the cast and 0.5 per cent acetic acid in small quantities was used to moisten the dressings once daily, with good results.

With mild infections of other invaders, sulfanilamide was sprinkled over the wound and sulfadiazine given by mouth. In our recent cases, however, we have used only penicillin, 25,000 units every 3 hours, continuously at the first sign of fever or purulent exudate. Meanwhile, skin grafting continued.

When the subcutaneous tissue became involved, phlegmonous, and swollen, wet dressings of moist, warm boric acid solution were used. Pressure dressings as before were used except that muslin or ace bandage was used for a cover instead of plaster of Paris. Skin grafts under this treatment did not take as well, but were continued because the results were still better than 50 per cent successful.

Tub baths were not available.

Sulfadiazine cream strips were not used in the presence of exudate from infection because it was felt that a nongreasy dressing would better absorb the material. Neither was this considered a good dressing over freshly laid grafts because of the possibility of causing the sections to slip.

BLOOD REPLACEMENT

None of the patients with first and second degree burns required transfusions. All had plasma, 1 unit for each 5 per cent of body surface involved.

Nine of the 26 patients with third degree burns required transfusions and a few required additional plasma. In general, it can be stated that patients with extensive burns will require blood. Four of our patients required 8 units (500 c.c. each) of blood. Three of these soldiers had 30 per cent body surface involved and the fourth had 40 per cent involvement. However, one man with 35 per cent body surface involved required only 1 unit. One soldier with only 10 per cent body surface involved required 2 transfusions, but he had considerable infection of a burned forearm. The other soldier getting blood received 1 unit.

Two patients required transfusions because of secondary bleeding after dissecting off extensive eschar. Areas from which the charred skin is removed bleed very little, so adequate precaution was not taken to prevent secondary bleeding. Mild pressure controlled the bleeding in both instances and the blood loss was promptly corrected by transfusion.

ANESTHESIA

In none of our patients was anesthesia used at the initial dressing. No débridement was done. Gentle cleansing of débris or street dirt was accomplished rapidly and almost painlessly whenever indicated. Coverage by sulfadiazine strips was done rapidly and the patient became comfortable with morphine, protection of burned surface, and immobilization.

However, all subsequent dressings were customarily done under pentothal sodium anesthesia. In patients who had only a small area of first and second degree burn, dressings were usually started without anesthesia and usually tolerated well. If much discomfort was experienced, anesthesia was promptly used. All patients were premedicated before being taken to the operating room for change of dressing. Usually the period of anesthesia was limited to 1 hour but a few were kept anesthetized for 1½ hours during grafting procedures. Usually patients anesthetized by pentothal sodium early in the day were hungry for lunch by noon, and always by evening they were ready for a full diet. This diet was important in individuals who were being grafted in stages, every fourth day. Pentothal sodium has been our most satisfactory anes-

thetic and was used in over 95 per cent of patients. No patient received over 2 grams at each period of anesthesia.

Three patients had gas oxygen ether anesthesia on one or two occasions when it was planned to do a long extensive grafting procedure with 3 surgeons at work. These periods of anesthesia lasted longer than 90 minutes; there were no complications, yet recovery of appetite and vigor was slow. Usually several days elapsed before the patient would take a full diet. Whether this was due to the anesthesia or the extent of the grafts might be questioned, but on several occasions we have done extensive grafting under pentothal sodium without ill effects. We have felt, therefore, that for this purpose the intravenous pentothal sodium is the outstanding agent because of lack of delay in inducing anesthesia and the rapidity of recovery of the patient to accept a full diet postoperatively. We used it liberally so that no soldier need dread either the change of dressings or operative procedures.

On several occasions when recipient sites have been small we have used local novocain infiltration for the donor site, but usually there were a few granulations on the recipient site to be trimmed down and some discomfort was experienced. As a result we have used local anesthesia only infrequently and only when a few small grafts have been needed.

EXERCISE

The problem of exercise or passive motion is very important in the treatment of third degree burns. In all of our first and second degree burns, bandages were removed and active motion started early enough to prevent any loss of function. Hand and finger motion in second degree burns was encouraged early. Splinting of hands was always with fingers in moderate flexion and thumb opposed. As much of the fingers as possible was left exposed and motion encouraged. When fingers were involved, either active or passive motion was used during the change of dressing.

In the third degree burns, passive motion of all joints in the involved area was exercised during the change of the dressings. Under anesthesia this was not difficult. Casts of extremities were put on with the knee in mild flexon, elbow in 90 degrees' flexion, forearm in neutral position, and hand and wrist in position of function with exercise at each dressing or operation.

GENERAL NURSING CARE

The nursing problem on the wards in the present method of treatment is much different from what it was when dressings were done on the wards. All dressings, without exception, were done in the operating room under strict aseptic technique. Therefore, the patient arrived on the ward as a package not to be opened. When hands were involved, these patients required feeding. Frequent change of position, when possible, was encouraged. Backrubs, bathing of uninvolved areas, and general hygienic care are important to these patients. Exercise of burned hands at the earliest possible moment was constantly encouraged by the ward personnel. Plasma and blood as needed were given on the wards. Rigid fly control during the summer season was supervised by the nursing staff. All in all, the nursing care of the wards was no more a problem with the burn patients than for an equal number of less severe battle casualties.

Most of our patients never had an opportunity to see their own wounds or those of the other burned patients until the wounds were completely healed or covered by grafting. They were kept comfortable and their morale was good due to the excellent attention of our nursing staff. Numerous letters received from those who have returned to the United States testify to the high regard for the nurses and ward attendants.

In the operating room, the change of dressings was done with the usual personnel. Dressings were usually saturated with saline after the removal of casts, the patient was anesthetized, and removal of dressings was continued painlessly and easily. None of the patients dreaded going to the operating room —in fact they felt neglected if their procedure was postponed a day longer than usual.

END-RESULTS

There were 2 cases, out of the 23 patients with third degree burns of the hands, who developed moderate stiffness of the fingers.

Both of these patients were treated early in this series when apparently not enough attention was given to exercise. Both were returned to the United States, one required a plastic procedure and remained in the service. The other reported to us recently that he was separated from the service because of partial disability of the left hand. He secured a job in a war plant and in a letter dated approximately 10 months after his injury he stated that he had recovered almost full use of his hand and was improving. At the present time all of our patients with hands involved are watched carefully and constantly encouraged to preserve hand function. There has been no more than a mild limitation of motion at any of the other joints, all of which should return to full function promptly. In fact, with the exception of the 2 cases mentioned with hand disabilities, all the remaining patients who returned to the United States went because large areas of newly replaced skin could not be expected to function well in the wearing of military equipment or stand the rigors of reconditioning and the trauma of combat. As far as we are able to learn, only the one patient has been separated from service. There were no fatalities.

SUMMARY

In this series of 155 cases no attempt was made to keep a complete record of events for later evaluation; there was neither time nor facility for research. No control group was used—rather, as changes in their management were made, the previously treated patients became the control group. By the end of this series we concluded that no change need be made in accepted surgical principles. Constant improvement of method and simplification of technique should, however, be the aim of the doctor who is treating burns.

The treatment of burns lies in the application of surgical principles to the wounds and the wounded. The wounded patient requires comfort, warmth, rest, and supportive therapy. The wound requires cleanliness to prevent sepsis, gentleness to prevent further trauma, coverage to prevent infection and allay irritation, support and pressure for comfort and to prevent fluid loss, immobilization for comfort, and lastly and most important, closure of the wound by skin in the shortest possible time to preserve the function of the deeper structures and prevent all the complications that occur in open wounds. The method used to accomplish these requirements is not too important, but any improvement of method that will hasten the accomplishment of recovery and avoid complications is a step forward. We have attempted to improve the method without evading the principle involved.

The treatment of this series of 155 burns represents the work of a group of individuals trained not as experts in the treatment of burns, but a personnel trained in the fundamental principles of management of wounds and wounded soldiers. The results have been gratifying and the following conclusions seem to be indicated.

CONCLUSIONS

1. Prompt, clean pressure dressing with immobilization is important in the treatment of burns.

2. Prompt administration of a calculated amount of plasma aids in the prevention of shock.

3. Infrequent dressing of burn wounds under strict aseptic conditions will help prevent infection.

4. Rapid skin replacement is the best method of preventing infection, deformity, and dysfunction in the presence of third degree burns.

5. Grafts transferred directly to recipient sites adhere well and donor sites do not become infected by working directly between donor and recipient sites.

6. Grafts placed immediately after removal of a charred eschar will grow well.

7. The use of passive motion under anesthesia will help prevent deformity.

ELECTROLYTIC ABSORPTION OF BONE DUE TO THE USE OF STAINLESS STEELS OF DIFFERENT COMPOSITION FOR INTERNAL FIXATION

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IN 1941, from a comparative study of stainless steel and vitallium (Key), it was concluded that 18–8 stainless steel and 18–8 S-MO, or enduro stainless steel, are practically inert in the tissues and are suitable for the internal fixation of bone.

It was further noted that the stainless steels mentioned exhibited a slight tendency to corrosion and that some other stainless steel nails which I had used in the past had exhibited considerable localized pitting, and one Smith-Peterson nail had corroded into two pieces after over 5 years but had caused no symptoms.

It was found that the vitallium nails and plates introduced by Venable and Stuck (4) exhibited even less tendency to corrosion or electrolysis in the tissues and in the solutions used in the experiments than did the stainless steels. But it was believed that the stainless steel possessed certain mechanical advantages which rendered it a more generally useful material for the internal fixation of bone than vitallium. It was stated that the Fracture Committee of the American College of Surgeons should recommend the standardization of 18–8 S-MO, or enduro stainless steel, for the manufacture of prostheses for the internal fixation of bone and should require such prostheses to be properly labeled in order that surgeons may know what type of stainless steel they are using. The prostheses should be passivated by the manufacturer.

The introduction of noncorrosive metals into surgery has led to a considerable increase in the use of internal fixation in bone and joint surgery and a number of new prostheses have been devised. Among those which I have found useful is the Neufeld nail (2). This is a two flanged nail which is bent to form an angle of about 135 degrees and continued downward as a slightly curved plate. It is useful in the treatment of trochanteric and subtrochanteric fractures of the femur. The two flanged nail is driven into the proximal fragment and the plate is fixed to the distal fragment with three self-tapping screws.

The appropriate screws are supplied with the plate and presumably they are of the same type of stainless steel as the plate. In order that corrosion with the attendant absorption of bone from electrolysis and consequent loosening of the screws and plate may not occur they must be of the same type of steel. Unfortunately, this is not always true, as is shown by the femora illustrated in Figures 1, 2, and 3. Under twilight and local anesthesia these fractures of the femur, 2 trochanteric and 1 subtrochanteric, were reduced by traction and internal rotation on a Bell table and under x-ray control the fragments were fixed with Neufeld nails.

The convalescences of the patients whose hips are shown in Figures 1 and 2 were uneventful except that the resorption of bone around the screws and under the plate was so marked that full weight bearing was not permitted until the Neufeld nails and screws had been removed, the cavities in the bones had partially filled in, and the bone increased in density to a point where it was believed that unrestricted weight bearing could be practiced with safety. The patient whose hip is illustrated in Figure 2 complained of persistent pain and disability until the nail was removed. It is also my opinion that union of the fragments, which was necessary before it was advisable to remove the nails, was delayed in all 3 instances. Repeated x-rays films of all 3 femora showed progressive absorption of bone around the prostheses, and as this fact was attributed to electrolysis it is believed that

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Fig. 1. Intertrochanteric fracture fixed with Neufeld nail. First operation June 20, 1944. Nine months after operation note marked electrolytic absorption around the distal screws and beneath the plate of the nail. On the right, the same hip is shown 2½ months after removal of the nail. Note marked regeneration of bone and more firm union at fracture site.

electrolysis was responsible for the delayed union in all 3 cases.

When the plates were removed from the patients whose x-rays films are shown in Figures 1 and 2, the screws were found to be corroded and loose. The wire which was used in the subtrochanteric fracture was real 18–8 stainless steel and this had remained bright and tight. The Neufeld nails were all bright, but they were not tight and the absorption of the femoral cortex which was present beneath the plates is clearly seen in all 3 roentgenograms. The same is true of the absorption of bone around the screws. In Figure 3, a relatively large area of absorption is apparent in the cancellous bone around the proximal and distal screws and union is delayed to such a degree that even now, 7 months after insertion of the nail, I do not think that it is safe to remove the nail and this patient is still on crutches. In the femora shown in Figures 1 and 2, the absorption of bone around the distal screws is so marked that a pathological fracture through the previously normal bone was a definite possibility. That this was entirely due to the prosthesis and not to infection or any other cause is evident from the increased strength of the bone evident in the x-ray films which were taken several weeks after the Neufeld nail and screws had been removed. On the basis of these x-ray films, unrestricted weight bearing was permitted and the patients seem to be getting along all right. The smallness of the bone, in the patient whose x-ray film is shown in Figure 2, is due to a partial paralysis of the extremity from old poliomyelitis. The nail in this patient was too long and protrudes into the acetabulum, but this caused no pain or disability. In addition to the absorption of the bone immediately adjacent to the prosthesis, there is some new bone production on the medial aspect of the shaft of the femur in the areas near the points where the screws projected, and even in the soft tissues around the projecting screws in Figure 3.

That the danger of electrolytic absorption of bone after internal fixation is not limited to the Neufeld nail is shown in Figure 4. This film illustrates the right hip of a girl, 17 years of age, in which the right femur was shortened 2¼ inches in order to equalize the length of the lower extremities. An arrest of growth had occurred in the distal epiphysis of the

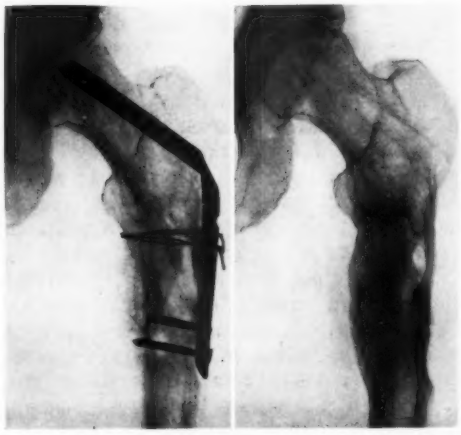

Fig. 2. Subtrochanteric fracture fixed with Neufeld nail and wire. X-ray films taken 5 months after operation. Note marked absorption beneath plate and around distal screws; also new bone formation on mesial side of shaft. On right is postoperative x-ray film a few months after operation. This patient had persistent pain and disability until the nail was removed.

opposite femur as a result of an osteomyelitis in early childhood. The postoperative convalescence was uneventful and she left the hospital 17 days after the operation walking on crutches. The hip remained painful but she had no other evidence of infection. In Figure 4 are shown x-ray films of the femur 3 months after the insertion of the blade plate and 2 weeks after its removal. The films show marked absorption around the plates and screws and considerable new bone formation. It is interesting to note that the absorption of the dense cortical bone around the two lower screws is proceeding even more rapidly than is that in the cancellous bone. At the second operation the fragments were united, the plate and screws were loose, and there was no evidence of infection. The convalescence was uneventful and the patient left the hospital on the 14th postoperative day on crutches with instructions to bear a moderate amount of weight on the leg.

Because of the danger of progressive bone absorption from electrolysis Venable (3) has warned against the use of vitallium and stainless steel screws or plates in the same operation or even in the same bone at different operations. The cases illustrated here indicate that the danger of electrolysis perhaps is even greater when different types of stainless steel are used.

Fig. 3. Trochanteric fracture 6 months after insertion of Neufeld nail. Union not yet solid. Note marked absorption in the marrow canal around screws and beneath nail, also new bone around projecting screws on inner side of shaft. Still on crutches; nail to be removed as soon as union is sufficiently advanced.

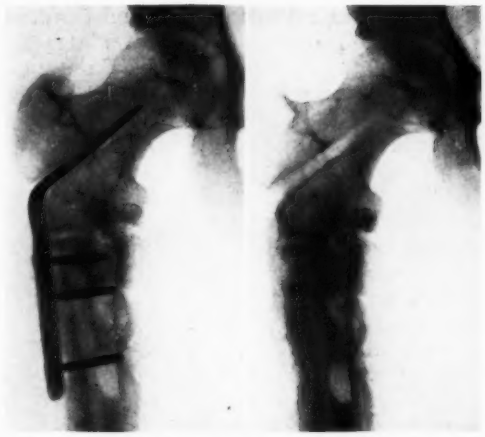

Fig. 4. Femoral shortening 3 months after fixation with Blount blade plate and 2 weeks after removal of plate. Note marked absorption, especially of cortical bone, around the two lower screws; also marked new bone formation.

Under present conditions it is necessary for the surgeon himself to be responsible for the quality of the prostheses which he uses for the internal fixation of bone. He cannot depend upon the hospital in which he works. Figure 3 illustrates the fact that the correct length of screw is not always available. Only a few days ago while I was applying a bone plate to a tibia, it was necessary to stop and check the screws in the Zimmer screw and drill rack. When purchased this rack was filled with an assortment of 18–8 S-MO stainless steel screws of uniform diameter and thread with the standard type of head. When checked, on the sterile instrument table, it contained some vitallium screws and 5 different types of stainless steel screws mixed indiscriminately, and the 1⅛ inch screws which were appropriate for the bone in this particular operation were missing entirely, their slot and an adjacent slot were filled with screws 1¼ inches long.

In addition to the heterogeneous mixture on the rack, there were probably a dozen other types of screws and plates in the operating rooms, some of which were purchased in 1912

when the hospital was opened, and this hospital is not unique in this respect. Plates and screws do not deteriorate with age and as new ones are developed, they are purchased and added to the stock, but the old ones are not discarded and they are all mixed together. The average operating room nurse knows nothing of electrolysis and its effect on bone.

In the light of what is known about the deleterious effect on bone of electrolysis caused by the use of metals of different composition for internal fixation, it is just as important that the metals used for internal fixation of bone be standardized as it is that drugs be of uniform purity and potency. And, when a prosthesis like the Neufeld nail, which is patented and the manufacture of which is controlled, is supplied with screws which are of different composition, what may we expect of prostheses which are purchased in the open market and are made by any one of a dozen or more manufacturers?

The surgeon can usually distinguish a vitallium prosthesis from one made of stainless steel, unless the former is polished, but he cannot differentiate stainless steels of varying composition at the operating table. It is again suggested that only stainless steel of a uniform composition be used for all prostheses which are to be used for the internal or external skeletal fixation of bone.

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A STUDY OF THE VALUE OF LOCAL SULFATHIAZOLE IN OPERATIVE WOUNDS IN THE PROPHYLAXIS OF INFECTION

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THE power of sulfonamides when administered by mouth or by vein to inhibit the growth of certain bacteria in the human body is well established. Although this method of therapy has had spectacular success in the treatment of many infectious diseases, such as lobar pneumonia, it has not been effective in preventing infection in accidental or surgical wounds. This may be due in part to the fact that many of the bacteria which cause wound infections are not susceptible to sulfonamides in the concentration that can safely be maintained in the body through systemic administration. Since many of these organisms are inhibited *in vitro* by high concentrations of the sulfonamides, it seemed logical to place the drugs directly in surgical and traumatic wounds. By this means a greater concentration of sulfonamide could be obtained in the wound than could possibly be achieved by systemic administration. This practice, first advocated in 1936 (6, 11, 13, 14, 32), has become so popular that many surgeons routinely place sulfonamides in their operative wounds.

Strangely enough, in spite of the extensive use of sulfonamides in human wounds for the purpose of preventing infection, there is little published evidence to prove that the practice is of value. Many of the workers who have claimed that the local use of sulfonamides decreases the incidence of wound infection either have not employed controls or have compared a sulfonamide-treated series with a control series treated one or more years previously (3, 5, 12, 15, 19, 20, 26, 27, 29, 30). This form of comparison often leads to fallacious conclusions (22, 24) because so many factors which influence the incidence of infection will vary significantly over these long periods. Those authors who have reported controlled series of cases have either reported only a small number of cases (4), or have not been able to confirm the opinion of those who believe that the sulfonamides prevent or decrease the incidence of infection when placed in operative or traumatic wounds (16, 23, 25, 33).

If a substance is recommended for application into wounds, the effects of the material on wound healing should be known. Critical evidence in regard to the effect of locally implanted sulfonamides upon wound healing is controversial. Animal experiments have shown that all the sulfonamides when implanted locally may produce an inflammatory reaction and even actual abscesses (34). It has been reported that retarded wound healing and extensive cutaneous scarring is to be expected with the local application of sulfonamides (1, 9, 35, 36). Others concluded that delayed healing is due to excessive amounts of drug locally, and stated that when used in proper amount, sulfonamides in no way retard healing or result in inefficient scar formation (4, 17, 18, 20, 21). After studies on humans, it was found that sulfonamides may act as irritants. It was demonstrated, however, that the deleterious effects are shortlived and that subsequent healing is within normal limits (28).

Because of this conflict of opinion, and because of the widespread use of these drugs in wounds, we undertook a study of our own to evaluate the use of sulfonamides locally as a means of preventing infection in operative wounds.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Wayne University.

From the Department of Surgery, Wayne University College of Medicine, and the Division of Surgery, Detroit Receiving Hospital.

TABLE I.—CLEAN WOUNDS

Bone operations	27
Minor surgical cases	99
Herniorrhaphies	74
Laparotomies	70
Total	270

TABLE II.—CONTAMINATED WOUNDS

Traumatic	126
Appendectomies	73
Perforated ulcers	33
Gastric resections	30
Bowel operations	33
Miscellaneous	11
Total	306

MATERIALS AND METHODS

Sulfathiazole was selected as the sulfonamide which, according to theoretical considerations, would be most likely to be effective in preventing infection. Two preparations were employed, sulfathiazole powder, and a 20 per cent suspension of microcrystalline sulfathiazole in saline (5, 7, 8, 31). The powder was sterilized before use by dry heat at 140 degrees Centigrade for 1 hour. The microcrystalline form was used as supplied by the manufacturer. All of the wounds were closed without drainage. Sulfathiazole was never "packed" in a wound, but a quantity just sufficient to "frost" the surfaces was spread evenly throughout the wound just before closure. Care was taken not to place sulfathiazole between the skin edges.

The patients, who were all admitted to one of the surgical services at the City of Detroit Receiving Hospital, were followed personally by the authors from the time of operation until wound healing was complete. Frequent inspections of the wounds were made, cultures were taken of any exudate, and the condition of the wound was noted and recorded on special summary sheets.

For purposes of study the series of 576 patients was divided into two main groups—patients with clean surgical wounds, and patients with contaminated wounds.

A clean wound was defined as one made deliberately by the surgeon and not contaminated during the operation by a bacteria laden material such as saliva, feces, or pus. The contaminated wounds were either traumatic wounds or operative wounds which were contaminated with infectious material during the operative procedure. Only traumatic wounds made with a sharp object and which could be débrided and readily closed without tension were included in the series. Subdivisions were made in each of the groups in order to make the wounds as comparable as possible. Patients in each of the subdivisions were alternated as drug treated or controls.

The subdivisions of the clean wounds were (1) wounds made for open reduction of fractures; (2) minor surgical procedures, such as lymph node biopsy; (3) wounds made for herniorrhaphies; (4) wounds for laparotomies. The subdivisions of the contaminated operative cases were (1) wounds made to repair perforated peptic ulcers; (2) wounds made for removal of acutely inflamed appendices; (3) wounds made for gastric resection; (4) wounds made for operation on the intestine; and (5) a miscellaneous group.

About 90 per cent of the operations were performed by 6 surgeons of the resident staff. The skin preparation, type of incision, and suture material were constant for each procedure.

Except for 14 patients who had sulfonamide therapy systemically because of pulmonary complications, none of the patients received any chemotherapy other than sulfathiazole in the wound. None of these 14 patients developed infected wounds.

RESULTS

The distribution of the cases is shown in Tables I and II.

TABLE III.—CLEAN WOUNDS

Drug	No. of cases	Infections	Per cent wound infections
+	128	5	3.9
o	142	3	2.1
Total	270	8	3.0

TABLE IV.—CONTAMINATED WOUNDS

Drug	No. of cases	Infections	Per cent wound infections
+	156	14	9.0
o	150	24	16.0
Total	306	38	12.4

Table III compares the incidence of infection in the clean wounds which were treated with sulfathiazole with those which received no drug. Five infections occurred in 128 drug treated patients making an incidence of 3.9 per cent; while only 3 occurred in 142 patients who received no drug, an incidence of 2.1 per cent. The incidence of infection in the two groups is almost identical.

A comparison of the contaminated wounds is shown in Table IV. In this series the incidence of infection in the patients who received sulfathiazole is less and it appears as though the drug exerted a beneficial effect. However, this difference is not statistically significant (2, 10).[1]

The wounds in which sulfathiazole had been placed were more indurated than the control wounds, and there was a higher incidence of hematoma in the drug treated group. These figures are given in Table V. Wound separation was rare, but occurred more often when the drug was not used locally.

Periodic tabulation of the cases and tabulation according to each surgeon demonstrated that the figures given in the tables were consistent throughout the study.

The organisms which caused most of the infections were Staphylococcus aureus, alpha, beta and gamma hemolytic streptococci and Escherichia coli alone or in combinations.

No definite evidence was produced to show that there was any difference in the effect of suspension of microcrystalline sulfathiazole or macrocrystalline powder.

TABLE V.—WOUND COMPLICATIONS OTHER THAN INFECTION

Type of case	Drug	No. of cases	Increased induration	Hematoma	Total	Complications per cent
Clean	+	128	19	6	25	19.5
Clean	o	142	7	3	10	7.0
Contaminated	+	156	16	2	18	11.5
Contaminated	o	150	10	3	13	8.6
Total	+	284	35	8	43	15.1
Total	o	292	17	6	23	7.9

EVALUATION OF STUDY

The statistics obtained from this study are reliable because the control series is comparable with the treated series. By classifying the patients into the various groups there tends to be only one important varying factor —whether or not sulfathiazole was used as local implantation in the wound before closure. There was no selection of cases for use of the drug. These are parallel alternating unselected controls.

Sulfathiazole when used locally in operative wounds just before closure caused an increase in the incidence of wound complications, notably increased induration with possibly delayed healing.

In heavily contaminated wounds sulfathiazole used locally seemed to decrease the incidence of infection but did not eliminate it. In clean wounds the incidence was not appreciably affected. The explanation of this divergence may be that in clean wounds there are not many bacteria and the incidence of infection is usually low. Here the foreign body reaction of the drug and its tendency to hematoma formation overshadow its antibacterial effect. In the contaminated wounds there are more bacteria and the natural incidence of infection is higher. Here the antibacterial effect of sulfathiazole is more important than its irritating effect on the wound and it decreases the incidence of infection. This treatment, however, is far from satisfactory as the incidence of wound infection is still 9 per cent. Furthermore, applying the principles of statistical methods, the difference in percentages of wound infections in the treated and control series, even in the contaminated cases, is not statistically significant and may be due merely to chance. Accepting this concept we could reconcile the findings in the clean and contaminated series. That is, there is no appreciable change in the incidence of wound infection brought about by using sulfathiazole prophylactically.

CONCLUSIONS

One can conclude from these results that sulfathiazole used locally in wounds does not prevent wound infection. There are several reasons for this conclusion.

[1]The statistical significance of the results were checked by Dr. Henry H. Pixley of the department of mathematics, College of Liberal Arts of Wayne University.

1. The organisms which cause wound infection are not very susceptible to the sulfonamides.

2. Dead tissue and foreign bodies, which are of necessity present to some extent in any wound, inhibit the action of sulfonamides.

3. Sulfathiazole leads to increased bleeding and hematoma formation, a factor known to predispose to infection.

These disadvantages together with their proved inability to prevent wound infection should lead us to seek other means of decreasing the incidence of infection in surgical wounds.

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VASOEPIDIDYMAL ANASTOMOSIS BY PRODUCTION OF PERMANENT FISTULA WITH USE OF STAINLESS STEEL WIRE

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AZOOSPERMIA as a cause of sterility in barren marriages is a common finding. Hotchkiss (4) found that 18.6 per cent of the men in his series of 100 infertile marriages showed no spermatozoa in the semen. In my series of infertile couples 13.3 per cent of the men had no spermatozoa in their semen, while in those couples in which the husband was either a contributing or a sole factor of the infertility the incidence of azoospermia was 26 per cent.

The absence of spermatozoa in the semen may be due either to failure of the testes to produce sperm or to blockage of the efferent ductal systems so that spermatozoa cannot pass into the semen. The etiology of this condition is often obscure. I was unable to determine it in 60 per cent of my cases.

The globus minor of the epididymis and the adjacent portion of the vas are the commonest locations for the obstructive type of lesion. Pre-existing localized inflammations probably account for the majority, though severe trauma is not an uncommon cause. Bothe and Robinson have described congenital strictures which if bilateral would cause azoospermia.

Gonorrhea is the specific disease which has most frequently been shown to be a cause of the obstructive lesion. Of course, such an infection must usually effect a bilateral blockage of the efferent ducts to produce an azoospermia. However, it is well to bear in mind that unilateral blockage can cause the same changes in the semen as that of bilateral lesions, if the opposite testicle is atrophic. Nonfunctioning spermatogenic tissue is a common sequela of cryptorchidism or mumps orchitis and occasionally follows severe trauma to the testis. Unilateral testicular atrophy, together with contralateral blockage of the epididymis or vas, will result in azoospermia.

It is worthy of note that the gonococcus never attacks the epididymis of an atrophic testicle. At least the author has not seen this occur, nor has any reference to it been noted in the literature.

Remedial therapy of sterility due to blockage of the epididymides or vasa, or both, has as its objective the re-establishment of the patency of the ductal passageways and the subsequent liberation of the imprisoned spermatozoa. In 1902 Martin devised an operation to accomplish this end. He united the vas with the epididymis using silver wire sutures, thereby establishing an anastomosis of the patent sections of each and bypassed the occluded areas. Hagner (2,3) pursued Martin's technique of vasoepididymal anastomosis and was able to report cures in 58 per cent of the cases in which the anastomosis was performed. Humphrey and Hotchkiss employed fine arterial silk as suture material. Hotchkiss (5) states "Successful results should reach about 20 per cent of those operated upon and yet the failures are no worse off than prior to operation." Nevertheless, most urologists have had so many failures with the Martin-Hagner method that commonly the sterile patient is advised against submitting to any surgical treatment.

Recently the author has devised and performed an operation for vasoepididymal anastomosis which appears to promise better chances for successful results. This operation is a modification of the Hagner-Martin method and introduces a new principle in that a permanent fistula is produced between the lumen of the vas and the globus major of the epididymis. This is accomplished by means of stainless steel wires[1] which are in-

[1]The use of stainless steel wire, as the least irritating foreign material both for sutures and for the production of the fistula, was suggested by Dr. Stirling Bunnell. Hotchkiss (5) suggests that nickel alloy wire may be used for the anastomosing material. He records that "Dr. John Draper has demonstrated that either silver or nickel alloy wire may remain in the lumen of the ductus deferentes of the dog for months without causing inflammatory reaction or foreign body response."

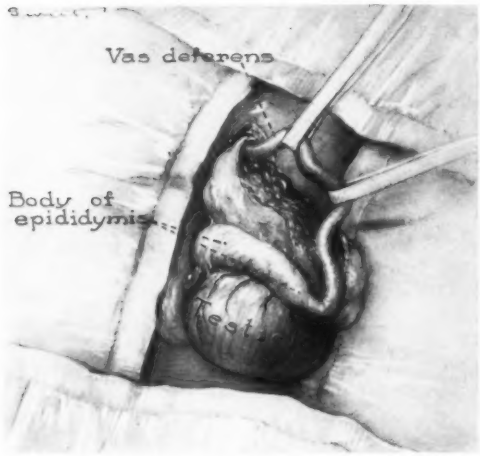

Fig. 1. The testicle, epididymis, and cord have been delivered from the scrotal sac. The vas has been isolated and is held up by umbilical tape. In this and the following illustrations the vas and epididymis have been drawn disproportionately large.

serted into the lumen of the vas through the incision for the anastomosis, passed upward in the lumen and out through its anterior wall, then brought out through the skin of the scrotum where the ends are fixed with shot. The lower ends of the wires are passed through the window cut in the globus major for the anastomosis and out the opposite side of this organ. They are then passed through the tunica vaginalis and the skin of the scrotum below the incision and fixed with shot. These wires are removed in 10 to 14 days. The steps of the operation are given in the following description:

Spinal anesthesia is the method of choice.

The scrotum and pubic region are prepared as for any intrascrotal operation. A longitudinal incision 5 to 6 centimeters long is made on the lateral anterior surface of the skin of the scrotum. The underlying layers of the muscle and fascia are incised, the tunica vaginalis is opened, and the testis, epididymis, and adjoining portions of the cord, including the vas, are delivered (Fig. 1).

The testicle and epididymis should be examined for any gross pathology. The vas is isolated and a convenient point is selected for anastomosis with the globus major of the epididymis. An oblique incision is then made across its anterior wall to expose the lumen. A dilute solution of methylene blue is injected into the terminal segment. A free flow of fluid will indicate that no obstruction exists distal to this point. A slight blockage might be overcome by the introduction of a strand of silkworm gut into the vas, thereby subsequently permitting the fluid to pass by the occluded point. If found obstructed at one site, it may be possible to perform the operation at a slightly higher level. Upon establishing proof of patency, the incision is then extended longitudinally and its margins are trimmed so that an oval window about 0.5 centimeter long is produced (Fig. 2). Attention is now turned to the epididymis, and an oval opening of approximately the same size is cut out of the lateral superior portion of the globus major of the epididymis (Fig. 3 C). The secretions from the excised tubule are immediately examined microscopically for spermatozoa. It is encouraging to demonstrate them in the epididymis at the point selected for anastomosis but the operation should not be abandoned if none is to be

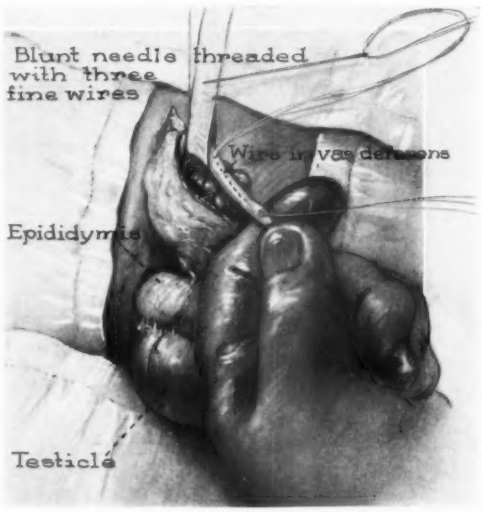

Fig. 2. A small incision has been made in the vas, and it has been enlarged and made oval in shape. Three wires threaded on a blunt ended needle have been passed through the incision, up the lumen of the vas and out through its wall.

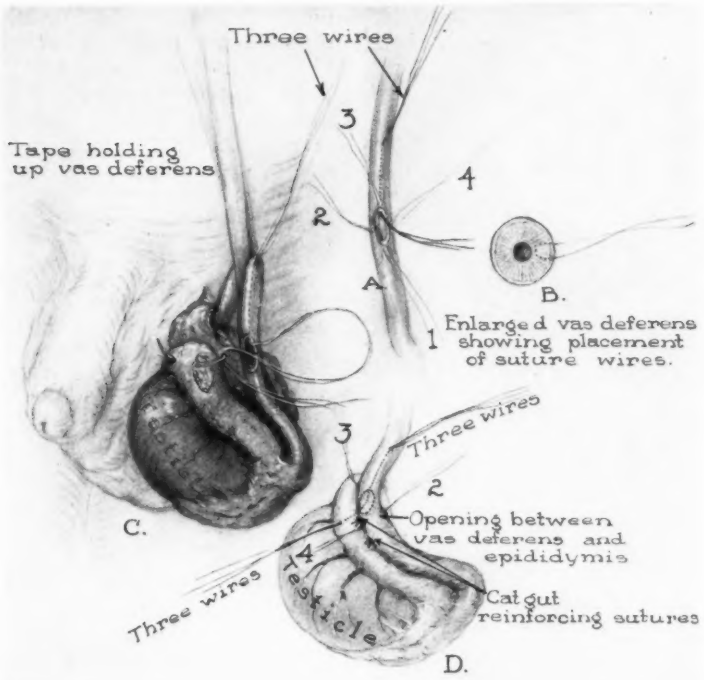

Fig. 3. A, The group of three wires has been passed through the oval incision in the vas, up the lumen of the vas, and out through its wall. The four wire sutures (*1, 2, 3, 4*) to make the anastomosis are shown. B, Diagrammatic cross section through the vas showing depth of anastomotic suture wires in its wall. C, The oval fenestra has been cut in the globus major. The needle carrying the fistula wires from the vas has partly been passed through the globus major. D, The anastomosis between the vas deferens and epididymis has been completed. The three wires which temporarily maintain the fistula are shown. Their course is indicated by the dotted line. The four anastomotic suture wires have been passed and tied. Three of them have not been cut and are shown.

found. This policy is substantiated by precisely such an experience on one occasion. Although a smear from the epididymis was negative a biopsy of the testis secured at the time of operation revealed spermatozoa to be present in the seminiferous tubules and ultimately they appeared in the semen, when it was examined after recovery from the operation (Fig. 5 a, b).

A blunt nosed straight cambric needle threaded with three stainless steel wires (No. 36, 20 to 25 cm. long) is then passed up the lumen of the vas for a distance of about 2.5 to 3.0 centimeters and then carefully pushed through its wall (Fig. 2). The needle is removed and the wires are threaded on a cutting skin needle. The lower ends of these three fistula-producing wires are then threaded on a suitable size Ferguson needle and passed through the window cut in the globus major and out the other side of the epididymis (Fig. 3 C). The wires are then threaded on a curved skin needle and left loose. At the margins of the incision in the vas, four stainless steel wire sutures (40) are passed through its wall, but not into the lumen. (Fig. 3, A,B). One each at the superior and inferior angle of the incision and one each midway laterally. These sutures are then passed through the tunica vaginalis, and several loops of the epididymal

Fig. 4. The operative wound in the scrotum has been closed. The mattress sutures are not shown. The ends of the group of the three fistula maintaining wires have been brought out through the scrotal skin and are held in place by shot. These wires are removed in 10 to 14 days postoperative.

tubule at corresponding points on edges of the window, already cut in the globus major. The inferior and posterior lateral sutures should be approximated and tied first, then the upper and anterior lateral sutures. One or two sutures of catgut fix the vas to the epididymis about 0.5 cm. to 1.0 centimeter below the anastomosis (Fig. 3 D). The testis and other structures are then returned to the scrotum.

The lower ends of the fistula-producing wires which have been threaded on a skin needle are passed through the tunica vaginalis and the skin of the scrotum about 2.0 centimeters below the end of the incision in the scrotum. Similarly the upper ends of these wires are passed about 2.0 centimeters above the upper end of the scrotal incision. The tunica vaginalis is sutured with catgut after first the introduction of an exploring finger to make sure that the organs are in proper position. The incision is closed with deep mattress sutures of silkworm gut and the skin with a running catgut suture. Before the incision is closed, it is advisable to measure on the wires where the shot should be applied so that there will be no tension. Following the closure of the skin incision both the lower and upper ends of the wires are shotted separately (Fig. 4). Tincture of benzoin com-

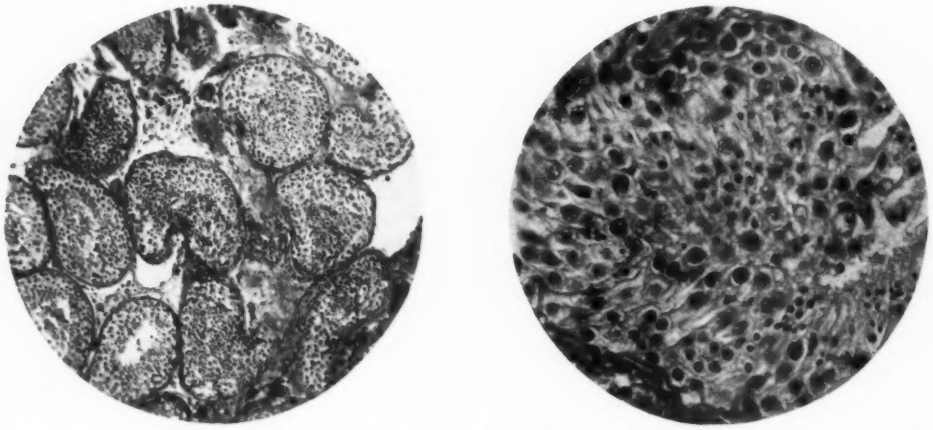

Fig. 5. Biopsy of testis. Case of azoospermia; duration 8¾ years. a, left, Low power. b, right, High power. Normal testicular tissue. The very small black bodies in tubules are spermatozoa. Spermatozoa absent in smear from epididymis at time of operation. Active spermatozoa present in ejaculated semen specimens which were taken during postoperative period of 1 to 7 months (last examination).

pound, gauze, and a large sized suspensory are applied with plenty of gauze for pressure.

The fistula wires are removed in 10 to 14 days without any difficulty. Convalescence in all cases has been uneventful.

The patients have had no serious pain and no complications have occurred. The swelling of the soft tissues remains 3 to 6 weeks. After 3 to 4 weeks the site of the anastomosis can be felt as an indurated mass about 2.5 to 3.0 centimeters in length and about 1.0 centimeter in width. This mass gradually subsides until in from 2 to 4 months it shrinks to a small, hard body about 1.5 by 0.6 centimeter. There is very slight tenderness on pressure and the patient experiences very little if any, discomfort after the first couple of weeks.

With the exception of this area of anastomosis, in all cases the testes, epididymides, and vasa appear grossly normal. As there has been no occasion to explore the patients operated upon, no microscopical examination has been possible. In experiments upon dogs, the author found no changes in the testes, although small fibrotic areas were found in the globus major, with fibrotic occlusion of the vas at the anastomotic area.

This operation has been employed in 5 cases of azoospermia due to blockage of the ductal systems. The gonococcus had been the primary causative agent in 4 cases, whereas the fifth was traumatic in origin. Bilateral occlusion was present in 4, while the fifth had unilateral testicular atrophy with occlusion of the epididymis on the opposite side.

The operation was completed on both sides upon 2 of the men, and in the remainder the anastomosis was done on one side only.

Spermatozoa have been found in the semen following operation in 2 of the cases. Atrophy of one testicle precluded the performance of a bilateral anastomosis in one of these patients. There has been one pregnancy.

The types of cases which have failed to demonstrate spermatozoa in the semen are as follows. The number of weeks postoperative that the semen was last examined is given.

Type 1. Patient suffered from postgonococcal bilateral vasoepididymitis. Operation was performed November 7, 1944. Bilateral anastomosis was done. Semen was last examined 3 weeks after operation.

Type 2. Patient suffered from postgonococcal bilateral vasoepididymitis with unilateral completely occluded vas. Operation was performed January 30, 1945. Unilateral anastomosis was done. Semen last examined 11 weeks after operation.

Type 3. Patient suffered from post-traumatic bilateral occlusion. Operation was performed October 31, 1944. Unilateral anastomosis was done. Semen was examined 26 weeks after operation.

Spermatozoa may appear in the semen any time up to the twelfth postoperative month and therefore the procedure cannot be completely evaluated until 1 year has passed.

SUMMARY

Five cases of azoospermia due to blockage of the ducts of the vas and epididymis are herein reported. A new operation is suggested in which stainless steel wires are interposed in the fenestra of the vasoepididymal anastomosis to further the development of a permanent fistula between these two structures. The series of cases is small but the percentage of successes is comparatively high. With further development of the technique it is hoped that more favorable results may be achieved.

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THE TREATMENT OF VARICOSE VEINS

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GROWING experience with varicose veins of the legs gives rise to more accurate understanding of this condition and makes possible the expansion and refinement of therapy. The treatment of 200 private patients seen since January, 1943, forms the basis of this paper. All the details of diagnosis, treatment, and follow-up have been carried out by me. It is my belief that this continuity of supervision tends to give the best results. Most clinics have to overcome the difficulty of insufficient personnel and an ever changing house staff. In addition since their clientele is from the lower income groups the staffs must constantly surmount ignorance, poor hygiene, and lack of co-operation. To a large extent these factors can be discounted in the present study.

Many of these patients present a superficial sameness which not only dulls interest but stifles critical appraisal. One can only say that careful examination and choice of treatment bring gratifying results.

ANATOMICAL

There are three vein systems in the leg (6): (a) the short or external or lesser saphenous, (b) the long or internal or greater saphenous, (c) the femoral or "deep" circulation. There is also a variable network of syperficial veins, particularly about the knee, thigh, and buttocks which can become varicose under certain conditions. These varicosities are not always associated with valvular deficiencies hence, in certain cases, saphenous ligation is not indicated.

PATHOGENESIS

Absence of valves. Studies in cadavers by Eger and Casper showed absence of valves in the external iliac and femoral veins proximal to the orifice of the saphenous in 36.8 per cent of cases. In this series one or both sides were deficient in valves, the left side approximately twice as often as the right. No attempt was made to correlate valve deficiency to the presence of varicosities. The conclusion that "on an anatomic basis there is a 36.8 per cent minimal potential incidence of varicose veins of the lower extremities" is an interesting hypothesis.

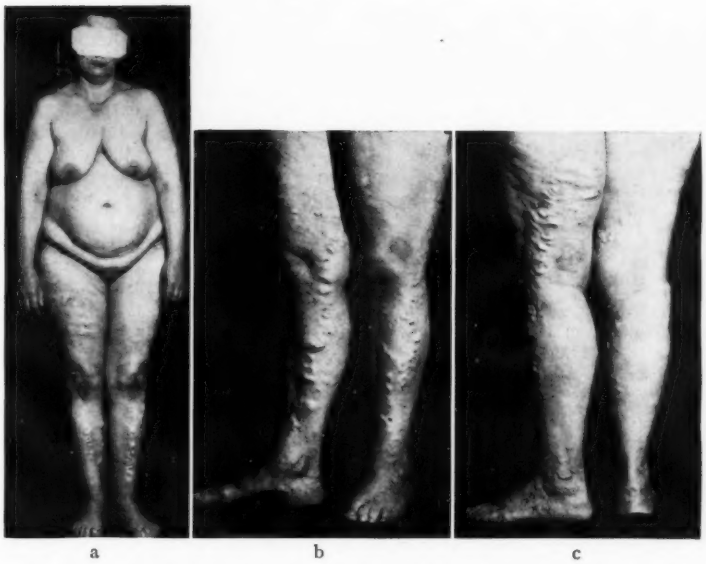
Valve incompetency. Routine tests for valve competency are applicable to any segment of vein one wishes to study. They do not permit distinction between developmental absence and acquired deficiency. It seems reasonable to assume that normal veins subjected to continued abnormal stress could be dilated to a point where the valves no longer close. This frequently happens in individuals following femoral phlebothrombosis when the superficial veins serve as dilated collaterals. Once the valve rings are stretched, incompetency increases, even after recanalization of the thrombosed vessels. Occasionally, however, I have found valve incompetency in the perforating veins—"blowouts"—which disappeared following bedrest and elevation, only to return on prolonged, unsupported standing. The moral of this is to examine thoroughly for "blowouts" when the patient is first seen. At this time the veins are usually biggest and the maximum number of "blowouts" can be discovered and marked for excision.

Valve incompetency exists most often at the greater saphenofemoral junction—making necessary the classical saphenous ligation. Usually this incompetency exists when the greater saphenous system is varicose. Occasionally the saphenous vein at operation is small and normal in appearance. In such cases there is usually a "blowout" farther down the thigh—sometimes only 2 or 3 inches below the saphenous bulb.

Another frequent point of incompetence is at the orifice of the lesser saphenous vein. This condition may exist by itself or be associated with greater saphenous varices. Incompetent valves in the perforating veins usually do not exist without one of the valvular defects above noted.

Venous pressure in standing individuals is the same in "normal" as in varicose veins (5). It corresponds roughly to the hydrostatic pressure of the blood column leading to the heart. In the recumbent position, in *both* antecubital and saphenous veins, pressures are elevated in patients with large varicosities. This is probably due to increased blood volume caused by partial emptying of the capacious varicose reservoir. The abnormality is corrected by proper treatment. Orthopnea in patients with mild degrees of heart disease is frequently relieved by proper attention to varicosities.

When the veins are full, as in the erect posture, blood flow in varicosities is upward, although slowly, as may be shown by venography. The

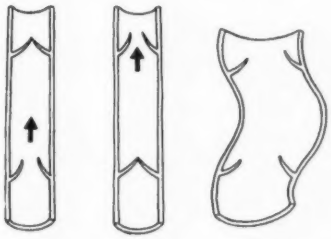


a b c

Fig. 1. a, Deficient vascular type showing bodily configuration. Note irregular, mottled skin. b, Same patient. There are varicosities of the right greater saphenous system. c, On the left side the varicosities arise from a "blowout" in the upper posterior thigh. Neither saphenous system is involved. Note telangiectasia about ankles.

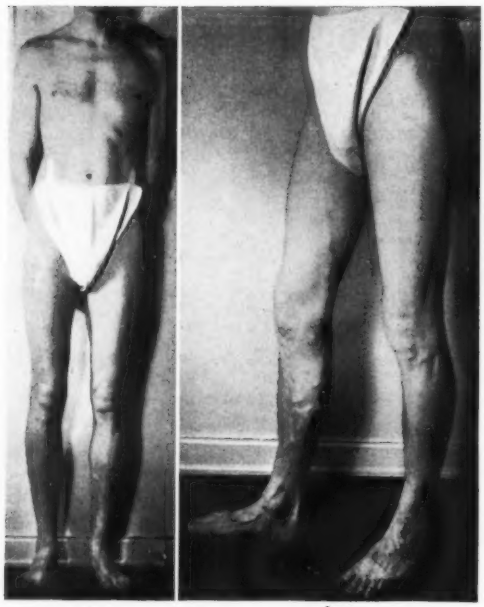
idea that blood flows out of the fossa ovalis and down the saphenous vein is erroneous and implies a pressure differential that does not exist. In *normal* veins the flow is rapid because of (1) the smaller caliber and (2) muscle action. The latter compresses a vein segment between two valves, blood flows through the upper valve which closes when compression ceases, and the segment again fills from below. When valves do not function this progression is not maintained and the blood stagnates (Fig. 2).

Constitutional factors. Empirical observations allow the segregation of some of these patients into groups according to body type. (a) *A deficient vascular group* (Fig. 1). In this group there is extensive superficial venous dilatation manifested by capillary hemangiomas, telangiectases, and a multitude of small varicosities. The legs are usually large out of proportion to the rest of the body. Sometimes there is immense adiposity of the buttocks, thighs, and legs suggesting glandular dysfunction. The larger vessels when exposed at operation are thin walled and tremendously dilated. There may be saccular bulges up to 4 or 5 centimeters in diameter. There may be associated hemorrhoids or vulvar varicosities. The overlying skin is irregular and mottled, becoming easily discolored. I have seen this type more often in females but frequently in males of the Froehlich habitus. Treatment is apt to be prolonged, difficult, and unsatisfactory. (b) A type apparently *deficient in connective tissue* (Fig. 3). This individual is usually male, lean, muscular, of athletic type with a long spare build. In him varices appear in early adult life and gradually enlarge through the years. He has little sub-



a b c

Fig. 2. a, Normal segment of vein between two competent valves. Upper valve closed, supporting blood column while segment fills from below. b, Normal vein segment. Muscle action compresses segment, partially emptying it; lower valve holds tight. c, Varicose segment. Valves incompetent. Muscle action can force blood in either direction. Upward flow not accelerated.



a b

Fig. 3. a, Type deficient in connective tissue. Long, spare build. Bilateral enlarged external inguinal rings. Small left direct inguinal hernia. Small right varicocele. b, Same patient. Saphenous enlarged from groin to internal malleolus. No other varices. Other leg normal.

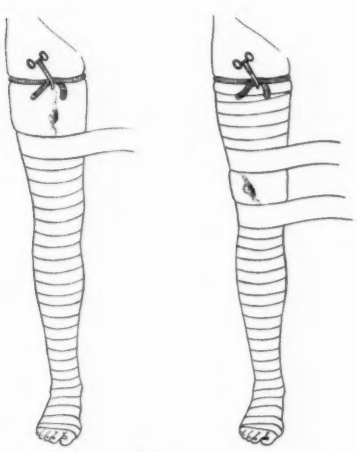
cutaneous fat so that all his veins are prominent. He may have an associated varicocele and is subject to inguinal hernia. Telangiectasia and pigmentations are uncommon. Treatment is more easily carried out and results are generally good. (c) *Congenital venous abnormalities.* These enlarged veins may be associated with other stigmas such as extensive hemangiomas. They are characterized by abnormal vascular connections and extensive valve deficiency. I have seen a patient with the entire right lower extremity covered with capillary hemangiomas extending onto the abdomen and buttocks. The enormously dilated right saphenous vein passed over the right fossa ovalis across the pubes and drained into the left femoral through the left fossa ovalis. There were numerous free connections between the abnormal vein and the right femoral vein. This type of varicosity is evident at birth or at a very early age.

DIAGNOSIS

The first step is to decide which venous systems are involved. According to Larson and Smith the *lesser saphenous* valve was incompetent in 7 per cent of 491 cases. Obviously if this is the only venous abnormality, other ligations are not necessary. A large vein or veins appear in the popliteal space near the flexion crease, and the associated varices involve the calf and ankle. If there is incompetence of the saphenofemoral valve, the greater saphenous vein is usually enlarged and may be palpable throughout its course down the inner aspect of the thigh, behind the internal condyle of the femur, ending in varices involving the medial and anterior part of the calf and leg. In very stout people it is difficult to locate the veins accurately. If there is doubt on this score, the greater saphenous vein should be ligated as a matter of routine. It may appear that neither vein pattern exists. In this case two situations may be present: either (1) there is *no* incompetence in the connections between the superficial and deep veins, or (2) there are isolated incompetent "perforators." In the first instance *no* ligations are necessary and in the second, routine saphenous ligation is useless. The "perforator" itself must be located and excised.

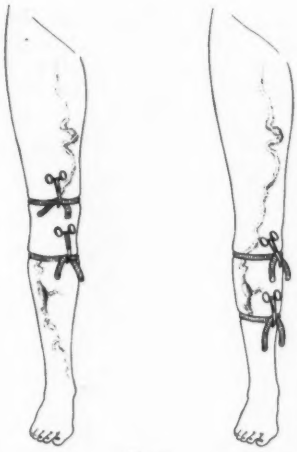
The patient to be tested for competence of the *saphenofemoral* valve rests supine with the leg elevated. Gentle massage in a proximal direction will hasten emptying of the veins. A tourniquet is applied high on the thigh firmly but not tightly enough to obliterate arterial pulsations. The patient then stands immediately. If the entire system of varices remains empty and then begins to fill slowly from below, one can assume there are no "blowouts." The tourniquet is removed. If the veins then fill rapidly from above, incompetence of the saphenofemoral valve is demonstrated. (Note: This down flow of blood ceases when the venous reservoir is filled. The blood then flows slowly upward.)

If during the test described the veins fill rapidly while the tourniquet is in place it is presumed that there is a "blowout" present. The level of the early influx of blood will give a clue to its location. To locate "blowouts" Pratt devised the following: "An Ace bandage is applied from the toes to the groin and a tourniquet placed on the thigh above this area. As the bandage is removed, a sudden protrusion of a collection of veins shows the point of incompetence. A second Ace bandage, which may be wrapped from above down, exposes only a small area at a time and is helpful" (Fig. 4). This is easily and quickly done. I believe, however, that the lower Ace bandage keeps the varices only partly empty, that, as it is unrolled, blood fills the visible portion of vein and that the blood may have come from below and not necessarily via a "blowout."



a Fig. 4. b

Fig. 4. a and b, Method of locating multiple blowouts using a tourniquet and two elastic bandages, (after Pratt).



a Fig. 5. b

Fig. 5. a, The leg has been elevated, thus emptying the veins, and a segment of vein isolated between tourniquets. The segment has remained empty in the erect position indicating an *absence* of blowouts in this segment. b, Test repeated with tourniquets reapplied lower down. Segment has rapidly filled indicating presence of blowout. Note: Veins below lower tourniquet remain empty, indicating absence of blowouts.

To locate these "blowouts" more exactly and to prevent the upward reflux from giving false positive tests for "blowouts," I make repeated application of the tourniquet at different levels, emptying the veins by elevating the leg between each application. The presence of a suspected "blowout" in any vein segment can be readily detected by using two tourniquets (Fig. 5). The vein is emptied and a tourniquet is applied on either side of the suspected site. If the isolated segment fills there is a "blowout" somewhere between the constrictions. By repeating the procedure, shifting the tourniquets, the "blowout" can be accurately located and marked.

Measurements. As a routine I measure both legs, selecting arbitrary points of reference. The ankles are measured at their slenderest level, the calves and thighs at a point 15 centimeters below and above the upper margin of the patella, respectively. Accurate comparison can be made later.

Perthes' test. This test is based on artificial occlusion of the superficial venous return by a tourniquet placed around the upper thigh. The patient then walks for 5 minutes. If the deep venous circulation is blocked, the leg becomes congested, swells, and is uncomfortable. This means that the superficial veins, both varicose and normal, are acting as collaterals. In this instance saphenous ligation is deferred until recanalization of the deep veins has occurred.

Tests for arterial disease. The dorsalis pedis and posterior tibial arteries are palpated as a routine. If these pulses are full, the arterial circulation is considered to be adequate. If palpation is difficult or impossible the arterial circulation *may* be normal since these vessels may show wide variations in caliber and location. Oscillometric readings are then done as an aid in determining the degree of arterial pulsation. The oscillometer should be used, of course, in all cases in which there is a history of claudication, abnormally cold extremities, or other history suggestive of arterial insufficiency.

Varicosities due to valve incompetence are treated by surgery even in the presence of advanced arterial insufficiency. Saphenous ligation with eradication of incompetent perforators is carefully done. Sclerosis is never attempted in the presence of arterial disease. Ace bandages are not worn postoperatively but rather all efforts are made to promote vasodilatation during the postoperative state. These measures include use of (1) a thermostatic heat cradle, (2) alcohol by mouth, (3) other vasodilators such as typhoid vaccine or depropanex, (4) mecholyl iontophoresis, (5) lumbar sympathetic novocain nerve block.

Laboratory data. Erythrocyte sedimentation rate. This is a valuable index of phlebitic activity. It should always be done if a history is obtained suggesting deep or superficial thrombophlebitis. Elevation of the rate may cause one to defer operation and certainly contraindicates the use of sclerotics.

Blood count. Certain patients have multiple episodes of thrombosis on the basis of polycythemia. Measures to bring the red cell count to normal should be taken before surgical intervention is undertaken.

X-rays. Venography has given valuable information regarding blood flow in varicose veins but has a limited application. It is valuable in demonstrating deep venous occlusion and may help to estimate some congenital anomalies. At best it serves only to confirm the clinical findings.

TREATMENT

Nonoperative Cases

If no valve deficiency can be demonstrated or inferred, it is useless to interrupt surgically any of the veins, varicose or normal. The cases falling into the nonoperative group show scattered, wandering varices of the superficial type, usually of medium caliber, but frequently in smaller veins and associated with telangiectasia. They are unsightly but rarely cause secondary effects, such as edema or ulceration. The treatment is by injection of a sclerotic. I use sodium morrhuate 5 per cent with benzyl alcohol as a routine and sodium ricinoleate 3½ per cent as an alternative in the rare case which shows sensitivity to the morrhuate. All patients should be given a preliminary test injection of 0.3 cubic centimeter of the sclerosing substance at the first visit. This injection is introduced into one of the varices and usually causes no reaction whatsoever. Very occasionally generalized urticaria results and even asthmatic symptoms develop. This situation should respond to an injection of adrenalin followed by ephedrine orally. I have never seen a true anaphylaxis. In two patients sensitivity developed to the morrhuate compound after a course of injections followed by 4 to 6 weeks' rest periods. The injections were discontinued because of mild, delayed urticaria. Ethylamineoleate has been tried but its effect seems less predictable and the sclerosis less firm and extensive than that from the morrhuate.

Injection is accomplished with a fine *sharp* No. 27 hypodermic needle. The patient stands—on a table with hand rails—so that the site of injection is roughly at the surgeon's eye-level. The light should strike the leg tangentially so as to silhouette the vessel. The syringe is held in one hand so that aspiration can be made when desired without changing the grip. Usually if the syringe is held downward, blood will flow into the solution without aspiration. The other hand serves to steady the tissues during the venopuncture. When one of these varices is excessively large, it must be emptied before injection is made. Too much blood dilutes the sclerosing agent, minimizing its effect. An excessively large clot forms, is painful, unsightly, and disappears slowly. To prevent this clot formation the leg is elevated after insertion of the needle and the vein is emptied before injection is begun. Sometimes this maneuver is difficult. When this difficulty arises, the patient lies supine and the veins are distended with the aid of a tourniquet which is removed after insertion of the needle.

From 1.0 to 2.0 cubic centimeters of solution are injected, depending on the size of the vein and the individual's reactivity. The latter varies considerably. The site of injection is compressed with alcohol soaked cotton wisps used for sterilization and maintained in position with two 4 or 5 inch strips of adhesive 1 inch wide. The length of vein sclerosed per injection is enhanced by the wearing of an Ace type bandage for 2 or 3 days. This bandaging keeps the sclerotic from "puddling" and spreads it along the vein while preventing influx of new blood. If this type of bandage is objected to a 4 inch square of cotton 1 inch thick applied over the injected area and bandaged into place for 48 to 72 hours may be less unsightly. Injections are usually made at weekly intervals. Sometimes four injections totalling 4.0 cubic centimeters are made in one sitting and are well tolerated.

Occasionally *palliative treatment* is the only sensible course. Operation is contraindicated sometimes by extreme age and often by other, more serious, illness. Measures taken include: (1) Ace bandages. These are put on before arising in the morning. For long continued use Ace type bandages, flesh colored, with elastic threads interwoven in 3 or 4 inch widths are most satisfactory. (2) If edema persists periods of *elevation* during the day and continuously at night are scheduled. (3) If there is a tendency to infection, daily hot saline *soaks* are instituted. Should there be evidence of a fungous dermatitis, warm potassium permanganate soaks 1:5000 are applied, daily at first, then alternately with the saline soaks, and finally at weekly or other intervals sufficient to control the situation. (4) *Dressings* for ulcerations usually are made with some bland ointment. I have no routine and often one must find the best applica-

tion by trial and error. Frequently, a plain dry dressing is the best, and this is soaked off daily. I have tried the various sulfa ointments, such as "Vitamin A and D" ointment, chlorophyll ointment, and others, and have found nothing for average use better than boric acid ointment. (5) *Weight reduction* in the presence of extreme obesity is important.

Operative Cases

Preoperative care is directed toward: (1) *reduction of edema*, and (2) *elimination of infection*. Generally the wearing of an Ace type of bandage with periods of elevation during the day and at night will suffice to reduce edema. For the most severe cases 1 to 2 weeks in bed at home may be necessary. It is hard to get co-operation from some individuals so that it may be necessary to admit them to the hospital 4 to 7 days preoperatively for close supervision. Hot saline soaks for infected ulcerations are carried out daily with appropriate dressings. These can be augmented by potassium permanganate 1:5000 soaks should fungous infection be present. In stout people weight reduction is begun immediately. The obese often have a troublesome groin intertrigo which must be cleared up before operation can be safely done. Frequent baths are followed by thorough drying, sprinkling with thymol iodide powder, and the insertion of gauze between the skin folds to keep the area dry. In cases of acute saphenous thrombophlebitis in which early ligation is to be done, it is my custom to give sulfadiazine several days before and after operation. This step is rarely necessary following femoral thrombophlebitis because the time lapse between acute infection and operation is sufficiently long (6 to 12 months) for infection to subside. If sclerosis is to be done, a preliminary test injection of 0.3 cubic centimeter of sodium ricinoleate is made into a suitable varix.

The patient is admitted to the hospital the evening before operation. For high saphenous and "blowout" ligations, the skin is shaved from toes to umbilicus and a low enema is given. Nembutal 1½ or 3 grains is given for sleep and repeated the following morning 1½ hours before operation. Morphine sulfate 1/6 grain and scopolamine 1/150 grain are given 45 minutes before operation. Most patients will then sleep soundly during the operative procedure. Immediately before the patient lies on the table the location of "blowouts" is checked and the actual lines of incision marked heavily with indelible pencil.

Choice of operation. Patients showing incompetence of the saphenofemoral valve should have a *high saphenous ligation* with division of all tributaries. Incompetent perforators should be excised. *Retrograde sclerosis* after the method of Pratt is done in uncomplicated cases. Sclerosis is contraindicated: (1) following acute saphenous thrombophlebitis, (2) in the presence of vasospastic disease of the lower extremities—painful, moist, postphlebitic extremities with or without ulceration react unfavorably and sometimes alarmingly to sclerosis—(3) in the presence of obliterative or other peripheral vascular disease as, for example, arteriosclerosis or thromboangiitis obliterans, (4) following abnormal reactions to the test dose such as urticaria, asthma, severe local pain, or inflammatory reaction.

If the saphenofemoral valve is intact, it is only necessary to excise any "blowouts" which may be present or to ligate the lesser saphenous vein at its termination. I also excise many extremely dilated segments as these are obliterated with difficulty and may break down following retrograde sclerosis. If the saphenous vein is dilated throughout, I usually interrupt it just below or just above the knee even in the absence of "blowouts." This lessens the tendency to recanalization of thrombosed varices in the calf and leg.

Operative technique. Shoulder pieces are installed so that moderate Trendelenburg position can be used if desired. Many large varices remain distended when the patient is in the flat position. This distention is undesirable if retrograde sclerosis is contemplated. The excess blood dilutes and "puddles" the sclerotic and causes excessive clot formation. About 10 or 15 degrees of Trendelenburg position is sufficient to drain the venous channels and is done when necessary. This appears to be more easily done than the bandaging technique of Pearce. It also leaves the legs free for secondary ligation.

The operative technique is modified from that of Pratt. Local anesthesia with 1 per cent procaine hydrochloride is used. A point 1 inch (2.5 cm.) below and 1 inch (2.5 cm.) lateral to the spine of the pubis is selected and an intradermal bleb is made (Fig. 6). This spot should lie over the saphenous bulb and occupies the center of the incision. In obese people the inguinal fold may be considerably below this spot. It may even be necessary, as Dunlop suggests, to make the wound on top of the fatty apron. The line of incision, parallel to Poupart's ligament, is infiltrated and the area anesthetized through the original bleb by advancing and retracting the needle point fanwise through the subcutaneous tissue. If the point of the needle is in continuous motion it is not necessary to test for vascular penetration by

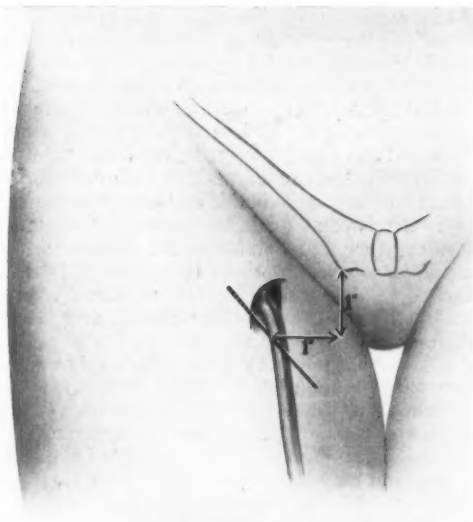


Fig. 6. Location of incision.

withdrawing the syringe. About 40 cubic centimeters of the anesthetic are generally used.

An incision 2 to 3 inches (5.0 to 7.5 cm.) long is made, depending on the thickness of the fatty layer. The operation is more quickly and safely done through an adequate incision. The vein is safely exposed by sharp dissection as traction is applied to the wound edges. Two layers of substantial superficial fascia are met and divided. In thin persons the deeper layer lies close to the vein. In the obese there is often considerable fat under this fascia through which the vein runs. Retraction is by means of spring self-retaining retractors. The vein is usually met at about the level of its lowermost tributary. It is dissected free from its bed. Exposure of the saphenous bulb is then completed by separating adventitia and fascia from the vein and dividing upward. This makes necessary a minimum of retraction (Fig. 7). In the majority of cases the superficial external pudendal artery crosses over the bulb. It serves as a landmark and may be divided if necessary. Often the artery passes next beneath the saphenous vein and occasionally it divides, sending small branches both over and under the vein.

The saphenous is freed up to its confluence with the femoral and all tributaries are divided between ligatures of No. 0 chromic catgut. From three to five are usually encountered. The saphenous is then ligated as high as possible with chromic No. 0 catgut. It is clamped distal to this and again 1 inch (2.5 cm.) lower. The intervening vein is removed. The proximal stump is secured with a C silk transfixion ligature distal to the first tie.

The distal stump is grasped laterally with clamps (Fig. 8) and the occluding clamp is re-

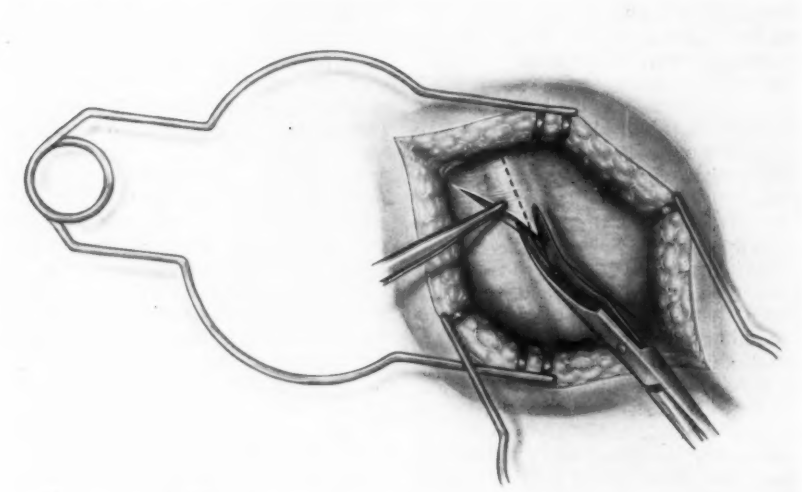


Fig. 7. Fascia divided upward along course of vein to facilitate exposure of saphenous bulb and ligation of tributaries.

moved. A ligature of chromic No. 0 catgut is readied with a half knot and a No. 6 French ureteral catheter is introduced into the vein. It will usually enter 25 to 50 centimeters without difficulty. Occasionally the tip catches in a valve leaflet or tributary opening. Partial withdrawal and axial rotation of the catheter will usually enable it to slide past these obstacles, but one must be careful not to push too hard as the vein wall is easily penetrated.

This procedure must be done quickly as the vein goes into spasm almost immediately. If the catheter becomes blocked and must be withdrawn reinsertion is almost impossible. When the catheter is at maximum insertion the half knot is tightened to prevent regurgitation, and wet saline sponges are packed about the vein opening to prevent any back flow into the tissues. From 3.0 to 10.0 cubic centimeters of 3½ per cent sodium ricinoleate solution are injected, depending on the size of the varices and the depth of insertion of the catheter. Twenty-five per cent of the sclerotic is first injected and the remainder is distributed uniformly along the course of the vein as the catheter is withdrawn. Occasionally, one is unable to penetrate further than 20 centimeters or so, even in the presence of a large saphenous vein. This is usually due to excessive tortuosity. The sclerosing solution can then be distributed distally by means of a gentle, sweeping massage while it is being injected. A larger amount can be introduced with safety and more complete sclerosis obtained. The knot is completed and reinforced with a C silk transfixion applied *above* the catgut tie. (If the vein is penetrated below this, the sclerosing solution will leak.) The wound is irrigated with saline (Fig. 9). Several interrupted fine catgut sutures are placed in the superficial fascia and the skin is united with interrupted silk vertical mattress sutures.

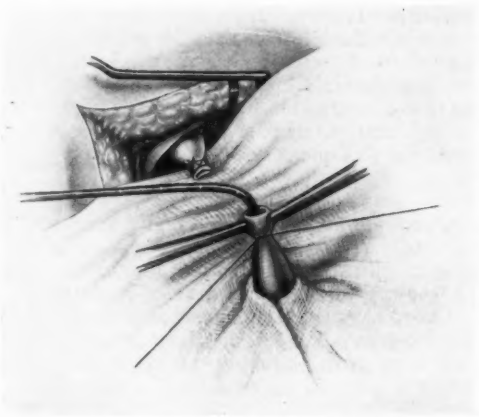


Fig. 8. Technique of retrograde sclerosis. Half knot prevents reflux.

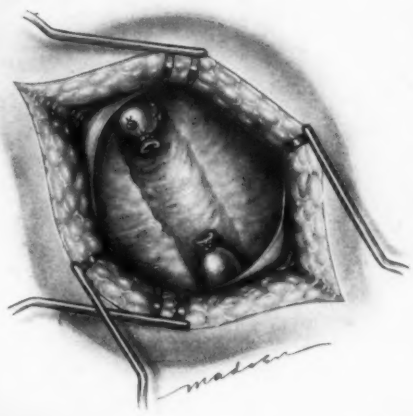


Fig. 9. Operative site ready for closure. Thoroughly irrigated with saline.

While the assistant closes the wound the surgeon attends to the "blowouts." The previously marked lines of incision 1 to 2 inches long are heavily infiltrated with 1 per cent procaine. This infiltration serves to separate superficial veins from the skin to which they closely adhere following phlebitis or chronic dermatitis and edema of long standing. The skin is cleanly incised and retracted with small rakes. Allis clamps necrotize the skin and should never be used to grasp skin edges. The vein is grasped, freed, and all available tributaries are clamped and divided. The T shaped junction between vessel and perforator is sought. The vein is divided above and below between clamps to prevent escape of the sclerosing solution. Should any escape, the wound must be immediately flushed with saline. The vessels are tied with No. 00 plain catgut. Chromic catgut was found to be poorly absorbed by this thickened, poorly vascularized tissue, particularly in the lower leg. The wound is closed loosely with two or three vertical mattress silk sutures.

Ligation of the lesser saphenous is accomplished in a similar fashion (Fig. 10).

Dressing must be carefully done. The femoral incision is entirely sealed with adhesive, especially in women. The lower gauze dressings are held in place with diagonal rather than circumferential

a b

Fig. 10. Varicosities of lesser saphenous system. a, Posterior view. Large venous channel marked where it lies beneath fascia. *X* marks site of ligation. b, Oblique view. Note enlarged greater saphenous coursing down medial aspect of knee. An excellent result was obtained in this case by ligating and sclerosing *both* greater and lesser saphenous veins.

strips of adhesive to obviate tension in the event of swelling. If retrograde sclerosis has been done, the femoral and leg regions, groin to ankle, are padded with combination dressings and the entire extremity bandaged firmly with two 4 inch Ace type bandages. If sclerosis has not been done, it is unnecessary to pad the leg but a 4 inch Ace type bandage is applied from toes to knee.

Postoperative care. Immediately the operative dressing is finished the patient is made to walk for 5 to 10 minutes. This distributes the sclerosing solution more evenly, enhancing its effect. "Puddling" is prevented and danger from vein breakdown and its attendant difficulties is minimized. Following this, the patient goes to bed. Thereafter he is required to walk 10 to 15 minutes every 2 hours until he becomes completely ambulatory. The outer bandages are removed after 6 hours and additional padding is placed over any point which seems unduly irritated. The padding is discarded after 3 to 5 days. The Ace bandages are replaced daily. Most patients go home wearing Ace bandages to the knee only. If the varices above the knee are large, it may be necessary to bind the thigh for 2 to 3 weeks. When retrograde sclerosis is done the average hospital stay is 4 days if one, and 6 days if both sides are operated upon. If simple ligation has been done, the patient usually goes home the following day.

The Ace bandages (or well fitting stockings) are worn for from 8 to 12 weeks or until sclerosis is complete, being removed only to bathe or when the patient is in bed. When sclerosis is complete the Ace bandages are discarded *gradually*. The legs will swell if this is not done as vascular tone takes time to return. I have the patient put on the Ace bandages as usual in the morning and wear them until late afternoon, when they are removed. If no swelling appears by bed time, the bandages are removed the next day in midafternoon. Thus the hour of removal gradually becomes earlier until the patient goes without bandages entirely.

Postoperative injections. Where simple ligation has been done, injections are begun as soon as the wounds are well healed, i.e., 10 to 14 days. Multiple (three or four) punctures at one visit can be made as tolerated. I do not inject more than 1.5 cubic centimeters in one place or more than 5.0 cubic centimeters at any one time.

If retrograde sclerosis has been done one should wait at least a month before injecting any remaining veins. Frequently no further injections are necessary. It is my experience that many vein segments not initially thrombosed will become so without injection during the first 4 weeks after operation. The average patient, however, needs 3 to 6 injections to complete the obliteration of the varices. I prefer to give an extra injection or two later than inject too much sclerosing agent at the time of operation. Pratt originally used 20 to 40 cubic centimeters of solution. I use about one quarter of this quantity.

Complications

1. Postoperative reactions. A febrile response to retrograde sclerosis occurs depending on (a) the amount injected, (b) the size of the varices, and (c) whether both legs are done. On the second and third days the temperature may reach 100.5 to 101.0 degrees F. Occasionally it is higher. This need occasion no alarm because better and more complete sclerosis occurs after increased febrile response. However, reaction higher than 103 degrees F. is considered abnormal. Although I have noted no permanent ill effects, these patients

should be watched closely. I have seen several instances in which the temperature reached 105 degrees F. on the third postoperative day and one instance in which it reached 107.4 degrees F. All these complications were either in postphlebitic patients or in patients who showed signs of heightened vascular irritability. These patients were kept in bed with the legs elevated. Papaverine, ½ to 2 grains, was given every 4 hours to lessen vascular spasm. Paravertebral novocain block was used in the more severe cases and extra fluids were administered. Possibly these reactions could have been avoided with proper selection of cases for sclerosis.

2. *Femoral thrombosis.* I have observed no case of femoral thrombosis—a fact attributable to the exclusive use of local anesthesia which makes the patient immediately ambulatory.

3. *Hemorrhage.* No serious bleeding has been encountered following the use of silk transfixion of the saphenous stump. Occasionally the femoral bandage becomes blood soaked during the period immediately after operation. This seepage of blood can always be controlled by pressure.

4. *Infection.* Avoidance of infection depends, I believe, on (a) the use of a single puncture wound for anesthesia, (b) delay of operation until dermatitis and other infections are cleared up, (c) avoidance of injury to enlarged femoral lymph nodes during operation, (d) prevention of contamination by proper dressing and the covering of the wound surface with sulfanilamide powder.

5. *Delayed healing of wounds.* Delayed healing of wounds frequently occurs without infection and only in the lower leg wounds. The lower the incision the more liable is healing to be slow. Healing is frequently delayed about the ankle when incision has been made through edematous, chronically inflamed skin. This difficulty is met with elevation, warm soaks, and suitable dressings.

Follow-up

The patients are seen at intervals after sclerosis is completed. The legs are inspected at the time the Ace bandages are discarded and again 3 months later. After this I see them at intervals of 6 months. Any visible additional varices can then be injected. New varices occur and are not to be mistaken for recurrences. Occasionally recanalization of certain channels occurs. This has been due usually to the presence of a blowout missed at the initial examination. Simple excision of the blowout followed by an injection or two remedies the situation.

SUMMARY

The origin of varicose veins is discussed and their anatomical types are enumerated together with the several types of bodily configuration in which varicose veins are most liable to occur. Different methods of treatment and their indications are outlined. Injection of veins and operative technique are discussed in detail. Contraindications to the use of sclerosing solutions include: (1) saphenous thrombophlebitis, (2) vasospastic disease of the lower extremities, (3) obliterative peripheral vascular disease, (4) abnormal reactivity to the test dose. Postoperative complications, their avoidance and treatment are described. Analysis of cases and late results will be the subject of further communication when more time has elapsed.

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ADENOCARCINOMA, CYLINDROMA TYPE, OF THE PAROTID GLAND

A Clinical and Pathologic Study of Twenty-One Cases

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In a previous study by two of us (Dockerty and Mayo, 4) it was pointed out that there occasionally arose in the submaxillary salivary gland a type of neoplasm variously known as cylindroma,[1] adenocarcinoma, cylindroma type or basal cell carcinoma with hyaline stroma. The incidence of this tumor, in a large series of submaxillary glandular neoplasms, was approximately 20 per cent. Throughout the literature as well as in our own series, this tumor had been confused with the ordinary type of mixed salivary glandular neoplasms. In this group of "cylindromas" recurrence was extremely high and metastasis frequent with more than 50 per cent of patients succumbing from the effects of widespread dissemination of the disease. Clinically, cylindromas could not be distinguished from the group of mixed tumors although pain was a contrastingly frequent symptom. Surgically, the infiltrative tendencies observed by the surgeon made him sometimes question a fresh tissue diagnosis of "cellular mixed tumor." However, in this previous communication distinctive microscopic features of cylindroma were presented and it was shown that the surgical pathologist familiar with the cellular pattern could render a real service in advising radical operative procedures when such a neoplasm was encountered.

More recent experiences (5) demonstrated that adenocarcinomas of the cylindroma type affecting the tongue and the parotid gland were also dangerous from the standpoint of metastasis. Mulligan, in a recent review, reported instances of 12 metastasizing mixed tumors, many of which had been primary in the parotid gland. Interestingly enough, most of the illustrations in his article duplicated the microscopic appearance of cylindroma in all major features. Since investigators still confuse mixed tumors with cylindromas and Bauer and Fox, on the basis of 3 tumors, stated that cylindromas are "genuinely benign," it was thought advisable to consider a group of primary neoplasms of the parotid to ascertain whether or not cylindromas occurred there and, if so, whether or not their clinical behavior was that of their submaxillary counterparts.

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Abridgment of thesis submitted by Dr. Quattlebaum to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of M. S. in Surgery.

After this paper was written Dr. Quattlebaum and Dr. Mayo entered the armed services and became Lieutenant and Colonel, respectively, Medical Corps, Army of the United States.

The term "cylindroma" whenever used in this paper appears as an abbreviation for "adenocarcinoma of the type cylindroma."

MATERIALS AND METHODS

Material was available on 210 consecutive cases in which primary parotid neoplasms had been removed surgically at the Mayo Clinic between the years 1928 and 1936 inclusive. This particular group of specimens was selected because it represented a series large enough to warrant conclusions as to the probable general incidence of parotid cylindromas and because it allowed ample time for a follow-up in the cases occurring in the later years of the series.

Before any records were reviewed, these 210 formalin-preserved tumors were carefully studied in gross detail, special attention being paid to the features of size, color, consistency, presence or absence of encapsulation, amount of parotid glandular tissue removed, presence of attached lymph nodes and so forth. Multiple blocks were cut from the tumors, the adjacent salivary gland, and regional lymph nodes when available. These blocks were placed in a 10 per cent solution of fresh formalin, sectioned at a thickness of approximately 10 microns and stained routinely with hematoxylin and eosin. Study of these sections brought to light 21 tumors which, although in many instances previously labeled atypical mixed tumors, seemed to fulfill the criteria for a revised diagnosis of adenocarcinoma of the cylindroma type. The present report deals with the clinical and pathologic details of this group of 21 cases.

PATHOLOGIC DATA

Gross features. In 19 cases the material was such as to suggest that total or subtotal removal of the tumor had been performed and in 2 instances

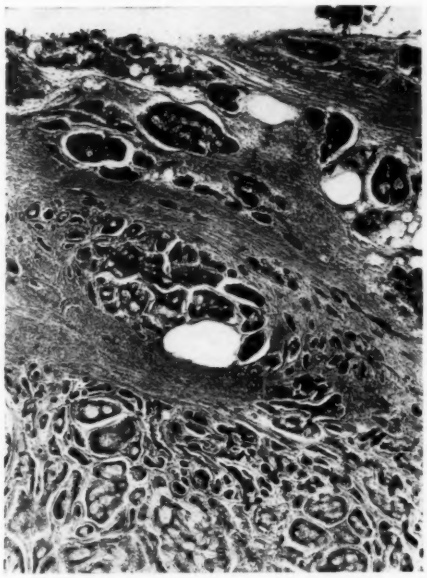

Fig. 1. Grade 2 adenocarcinoma, cylindroma type, illustrating resemblance to basal cell carcinoma. The honeycombed plugs of malignant cells are distinctive, as is also the hyaline stroma. The so-called capsule shown in the upper portion of the photomicrograph is extensively invaded by malignant cells (hematoxylin and eosin ×44).

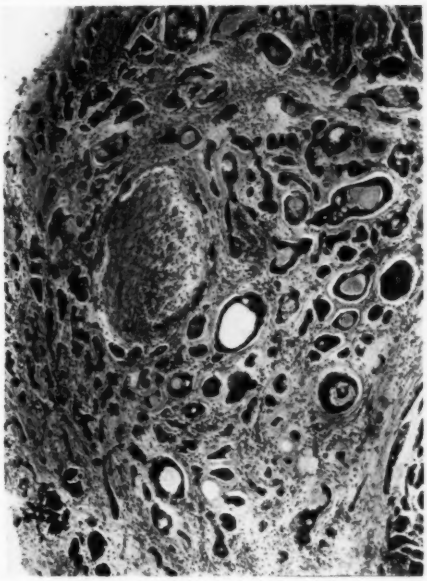

Fig. 2. Grade 2 adenocarcinoma, cylindroma type, illustrating again the basic architecture in addition to the phenomenon of perineural invasion by carcinoma cells (hematoxylin and eosin ×44).

only a small biopsy specimen was available for study. All of the tumors were unilateral. In 4 cases the entire parotid gland was attached to large neoplasms of an infiltrative type and in 2 additional instances the presence of attached, malignant appearing cervical nodes indicated that fairly extensive operations had been performed. In 7 of the remaining 17 cases the tumor appeared in the form of single or multiple grayish white encapsulated nodules. Rarely could the capsule be separated with ease from the underlying tumor tissue. Nonencapsulated examples always demonstrated invasion of attached parotid glandular tissue or the surrounding adipose connective tissue and portions of striated muscle which were occasionally removed with the operative specimen. In 1 case an attached portion of the mandibular ramus was grossly invaded by neoplastic tissue.

Microscopic features. The microscopic appearance of these tumors differed in no essential respect from that detailed in a previous study (Figs. 1 to 6). The general architecture was that of islands and strands of small dark-staining cells with hyperchromatic nuclei. Many of the units demonstrated central honeycombing with clear spaces which in some instances were filled with hyaline substance, in others were occupied by globules of material which stained positively for mucus and in still others were empty. The stroma was in general hyaline. Infiltrative tendencies were pronounced, the tumor capsule, the attached parotid glandular substances, the surrounding fat and so forth frequently demonstrating invading strands of tumor tissue running out from the parent growth. Perineural involvement was observed in all 11 instances in which nerve fibers were found. Metaplasia to epithelium of a squamous type was noted in 2 tumors. All the other neoplasms were pure adenocarcinomas of the type cylindroma, 14 being of grade 2 and 7 of grade 1 malignancy according to the method of Broders. In 2 instances portions of the neoplasm demonstrated appearances somewhat typical of mixed tumor. Previous experience had taught us that this group of "intermediates" ran the clinical course of cylindromas and accordingly they were included in the present series.

CLINICAL DATA

Incidence. The incidence of parotid adenocarcinomas of the cylindroma type was 10 per cent of the entire group. Stein and Geschickter observed

Fig. 3. Grade 3 adenocarcinoma, cylindroma type, illustrating marked cellularity, poor glandular formation and infiltration with splitting of the capsule. "Enucleation" in this case would have left behind multiple tumor seedlings (hematoxylin and eosin ×26).

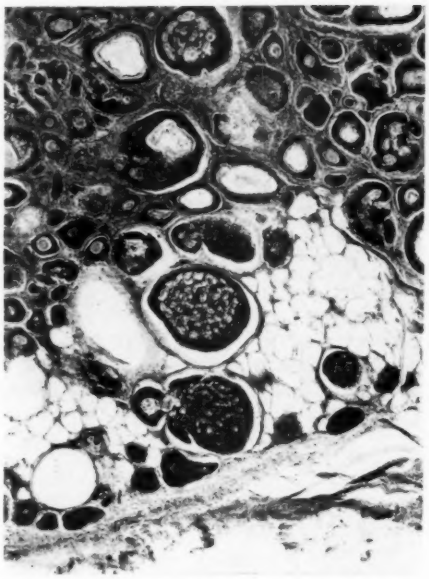

Fig. 4. Grade 1 adenocarcinoma, cylindroma type. In spite of good acinar formation and other evidences of cellular differentiation the infiltrative propensities are in evidence with the invasion of fat (hematoxylin and eosin ×44).

a 15 per cent incidence of this type. The corresponding figure for the submaxillary salivary gland was 18.5 per cent according to Dockerty and Mayo (4).

Sex. Men and women were almost equally represented in this series, in keeping with the observation in the literature that salivary glandular neoplasms have no particular sex predilection.

Age. The average age of the patients was 49.8 years with extremes of 32 years and 65 years.

Symptoms. The commonest symptom related by the patients was the presence of a tumor with an incidence of 100 per cent. The duration of the swelling varied from 6 months to 15 years with an average of about 7 years. It was thus impossible to judge, on the basis of this symptom alone, the nature of the underlying pathologic process.

Half of the patients additionally complained of pain, which was constant and localized in 2 instances and intermittent and lancinating in the remainder. Six patients had experienced extension of pain across the face, over the forehead or down into the neck, the character and distribution indicating irritation or actual invasion of a nerve by the tumor. In our experience pain was an unusual feature in connection with mixed salivary glandular neoplasms and its presence in patients suffering from primary parotid and submaxillary swellings should make one alert to a possible underlying adenocarcinoma of the cylindroma type.

On physical examination 10 tumors involved the right and 11 the left parotid gland. All tumors were unilateral. Location was generally described as being preauricular with certain tumors varying in occupying a high or a low position. The average estimated size was 4.5 centimeters with variations from 1 to 7 centimeters. Whereas 10 of the tumors were somewhat movable, resembling mixed tumor in this regard, the remainder were described as being fixed, a feature suggesting the presence of infiltration. As pointed out previously, local fixation of the tumor is an important sign in distinguishing adenocarcinoma of the cylindroma type from mixed tumors of the salivary glands. Partial or complete paralysis of the facial nerve was present in 25 per cent of the cases at the time of first examination at the clinic. Whereas in several instances it is possible that this paralysis follows the performance of a previous operation we feel on the basis of pathologic studies that it is most often brought about through perineural invasion of the seventh nerve.

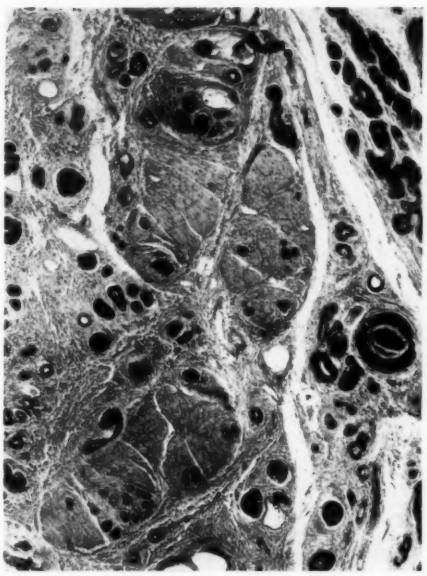

Fig. 5. Grade 2 adenocarcinoma, cylindroma type. This neoplasm was "recurrent" and illustrates extensive invasion of striated muscle (hematoxylin and eosin ×44).

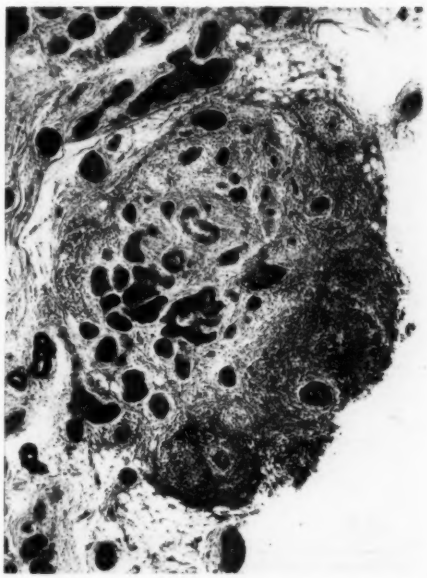

Fig. 6. Grade 2 adenocarcinoma, of the cylindroma type, with the invasion of a lymph node (hematoxylin and eosin ×44).

At operation only 39 per cent of the tumors were invested by anything which could be described as being a capsule, the remainder demonstrating evidence of infiltration. It was estimated that complete excision was accomplished in 50 per cent of the cases. However, several of the cases in which the surgeon made a note regarding residual tumor tissue were instances in which previous operation had been performed and the neoplasm was listed as a "recurrence."

TREATMENT AND RESULTS

Treatment consisting of wide local excision alone or combined with postoperative therapy using roentgen rays was employed in 15 cases. Complete parotidectomy was performed 4 times for large neoplasms, 1 of which represented a recurrence following a previous "local" operative procedure. In the 2 remaining instances biopsy followed by roentgen therapy was the therapeutic regimen dictated by the presence of an irremovable tumor mass. Fourteen of the patients received their first treatment at the Mayo Clinic. In 7 cases treatment instituted elsewhere was continued at the clinic because of neoplasms which had recurred.

Follow-up studies are available on 20 of these 21 patients and the detailed results are given in Table I. Although we have no necropsy data on the 10 patients who have died, presumption that death was owing to the effects of carcinoma is afforded by roentgenograms positive for pulmonary metastasis in 5 of the group and of cervical nodal metastasis in 2 additional cases. The 5 patients who are living without any evidence of recurrence represent a disappointingly small group (25 per cent). The 2 deaths and the 2 recurrences in the group subjected to total parotidectomy make a poor showing for an operation of such magnitude. However, these 4 patients were suffering from very large infiltrating neoplasms. Paralysis of the facial nerve was present in 25 per cent of the patients on their first admission. It developed in an additional 43 per cent at a time following operation, which indicated a causation based on infiltration by recurrent tumor in all except the 3 cases in which the nerve was purposely sacrificed in the operative attempt to eradicate large tumors.

COMMENT

Although adenocarcinoma of the cylindroma type occurs in all locations which provide the tissue of origin for mixed tumors of the salivary glandular type it is our firm opinion that there is no justification for including the two types within the same category. Histogenetically mixed tu-

TABLE I.—RESULTS OF TREATMENT IN CASES OF ADENOCARCINOMA, CYLINDROMA TYPE, OF THE PAROTID GLAND

Case	Treatment	Final results	Cases	Per cent
1	Palliative x-ray	Dead in 5 years		
2	Palliative x-ray and radium	Dead in 5 years		
3	Local excision	Dead in 5 years		
4	Local excision and radium	Dead in 5 years		
5	Local excision and x-ray	Dead in 5 years		
6	Cautery excision and radium	Dead in 5 years		
7	Parotidectomy and x-ray	Dead in 5 years		
8	Parotidectomy, x-ray and radium	Dead in 5 years		
Total cases (dead in 5 years)			8	40
9	Local excision and x-ray	Dead in 13 years		
10	Local excision and x-ray	Dead in 6½ years		
Total cases (dead after 5 years)			2	10
11	Local excision and radium	Living 8 years. 10 recurrences		
12	Parotidectomy and x-ray	Living 7 years. 6 recurrences		
13	Local excision and radium	Living 7 years. Last recurrence 4 years ago		
14	Parotidectomy and x-ray	Living 15 years 2 recurrences		
Total cases (living with repeated recurrences)			4	20
15	Local excision	Living 13 years (Status unknown)	1	5
16	Local excision	Living 7 years. No recurrences		
17	Local excision and radium	Living 7 years. No recurrences		
18	Local excision and radium	Living 8 years. No recurrences		
19	Local excision, radium and x-ray	Living 10 years. No recurrences		
20	Local excision, radium and x-ray	Living 14 years. No recurrences		
Total cases (without recurrences)			5	25

mors arise from the epithelial cells of the salivary and lacrimal glands and also from mucous glandular elements of the lip, tongue, palate, larynx, and trachea. The tumors are well differentiated, often reproducing in fair detail the double layering of epithelium which characterizes the appearance of a normal salivary duct. A cartilage-like stroma is typically encountered. In adenocarcinomas of the cylindroma type ducts lined by double layers of epithelial cells are lacking, the appearance being that of dark-staining honeycombed epithelial plugs. This may indicate, as suggested by Bauer and Fox, a derivation from the basal, basket, regenerative or "myo-epithelial" layers of the glands and ducts of origin. Cartilaginous stromal changes are not observed but hyalinization of the stroma is of frequent occurrence.

Clinically, "location and duration" are features which in a given case are by no means diagnostic of cylindromas as opposed to mixed tumor. The clinical incidence of pain, however, was 50 per cent in our group of cylindromas. In our series of submaxillary neoplasms pain had an incidence of 70 per cent as opposed to a 50 per cent incidence as a symptom of mixed tumor. Accordingly we feel that pain, especially of a sharp or radiating nature, is of importance in differential clinical diagnosis. Of parallel significance was the finding of fixation, which in our experience was a noteworthy feature of cylindromas.

At surgical exploration cylindromas were found to be infiltrative in more than half of the cases and rarely in these cases was the surgeon satisfied that he had completely eradicated the disease. That his estimate was correct is attested by a recurrence rate of 75 per cent, about three times the incidence for recurrence of mixed tumors (3). The question is therefore raised whether or not more radical surgical measures should not be undertaken for this more malignant cylindroma group. To most surgeons the mere mention of parotidectomy calls up at once the specter of a patient with severe facial palsy. However, the analysis of this series reveals that almost one-third of the patients had partial or complete paralysis of the homolateral facial nerve at the time of admission and this incidence reached two-thirds at the final analysis. That this figure is three or four times as great as the corresponding one encountered among patients operated on for mixed tumor (3) lends strong support to our pathologic observation that perineural involvement by tumor tissue rather than surgical trauma had been the factor responsible for the paralysis.

Admittedly if paralysis, complete or incomplete, of the facial nerve exists preoperatively, it is due to the perineural invasion or pressure of the tumor.

If paralysis develops immediately after operation it is due to surgical interference with the nerve. This paralysis may be partial or complete. If it is partial, it is usually due to tension or stretching of the nerve and slowly improves. If it is complete immediately, the paralysis of the nerve is likely to be surgical and permanent. In a small percentage of cases, however, complete paralysis may become partial and in a much smaller

number the patient may completely recover from it.

Paralysis developing a month or more after surgical resection can be safely attributed to incomplete eradication of the pathologic process and continued extension by infiltrating involvement.

Bailey has performed total parotidectomy for 7 parotid tumors with resultant palsy of the seventh nerve in 1 instance only, demonstrating thereby that surgical "interference" with the nerve can at least occasionally be avoided.[1] In the 4 cases in which total parotidectomy was done in the present series the facial nerve had to be sacrificed because of large infiltrating neoplasms. Subsequent recurrence in all 4 cases and death in 2 of them indicated to us merely that the operation was "too late" rather than "too little." It seems logical to assume that since resection of the gland, although usually effective in the treatment of mixed tumors, is followed in the cylindroma group by a 75 per cent incidence of recurrence, procedures at least approaching total parotidectomy should here be given a fair trial. We further feel that block dissection of cervical nodes on the involved side should be seriously considered. In this regard, as mentioned in the foregoing, the surgical pathologist familiar with the appearance of these tumors in "fresh frozen sections" can render a real service to his surgical colleagues.

While therapy with roentgen rays did not in the present series have any pronounced effect in the prevention or control of recurrences we feel that its possible benefits should never be denied to any patient suffering from this serious form of cancer.

SUMMARY AND CONCLUSIONS

1. Ten per cent of a series of consecutive primary parotid neoplasms appeared to be adenocarcinomas of the type cylindroma, so classified because of a distinctive microscopic pattern.

2. This group of 21 cases was characterized clinically by the presence of sharp radiating pain and local fixation of tumor in 40 per cent, features unusual in connection with other primary neoplasms of this location. Partial or complete paralysis of the facial nerve was also a contrastingly common finding.

3. Surgically, the tumors were generally more infiltrative than encapsulated and application of the principle of "wide local excision" prevented recurrences in 5 of 21 cases.

4. Pathologically, the appearance of dark-staining epithelial islands and strands with central honeycombing in a hyaline stroma was diagnostic. Epithelial mucus was sometimes present. Infiltrative tendencies were pronounced, with a special predilection for invasion of nerve sheaths.

5. Eight of the 20 traced patients succumbed within 5 years to the effects of metastasis, 5 with evidence of pulmonary spread. Two died more than 5 years after operation. Four of the remaining 10 are suffering from inoperable (?) recurrences.

6. Solid tumors of the parotid gland should be assumed to be malignant until proved otherwise.

7. It is suggested that more radical surgical procedures will have to be done in order to obtain better results in the treatment of this form of neoplasm.

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[1] McWhorter showed that the human parotid gland consists of a larger superficial and a smaller deep lobe usually distinct and readily separable. The facial nerve and its branches lie between these lobes and not within the actual glandular substance. The two lobes are joined by an isthmus which separates the temporofacial and cervicofacial divisions of the main nerve trunk.

A CLINICAL STUDY OF EARLY POSTOPERATIVE AMBULATION IN GYNECOLOGY

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WITH surgical efficiency at its present level, we should not be satisfied merely with recovery from a surgical operation, but we should know, as Matas once stated, "how the patient has recovered, to what extent she has been restored to her anatomical and functional integrity, to what extent she has been 'cured' and made fit to return to her normal life and occupation, how long it has taken her fully to recover after the operation, and what are the end-results."

"There is no excuse for leaving a single stone unturned to mitigate the suffering, shorten the convalescence, and eliminate the economic waste incident to surgery on human beings" (20), and, if early postoperative ambulation is an added means toward this end, then its use should be more widely adopted.

A comparison of the relative merits of early ambulation with those of late ambulation will be made in the following report. This presentation, may in effect, along with similar preceding reports (17, 22, 23, 25, 27), remove prejudice and add to the surgeon's postoperative therapeutic armamentarium. Of course, there are limitations and although this series was consecutively treated by early ambulation, the surgeon's judgment should individualize each case. However, the results demonstrate that fear of early ambulation is, in the majority of cases, unwarranted.

PRESENTATION OF DATA

Fifty-four consecutive cases are herewith discussed. The first 17 patients were maintained on the conservative regimen of late ambulation, the following 37 patients received early postoperative ambulation. No attempt was made to collect additional cases of patients treated by the old regimen because it was desired to maintain the factor of the operator constant. Because of this fact, no attempt will be made to quote percentages; only a relative comparison will be made.

Since the original compilation of this report, several additional patients were also treated by early postoperative ambulation with apparently similar results, but are not herewith included because of insufficient follow-up.

All patients were charity cases, from many sections of the State of Nebraska. All patients received adequate preoperative care. Patients with low blood counts and hemoglobin values received adequate transfusions.

The technique of operation was constant in both series.

Of the patients ambulated early, 7 had Pfannenstiel incisions, the remainder had midline incisions. All of the patients ambulated late had midline incisions.

In all total abdominal hysterectomies, 5 grams of sulfathiazole powder or crystals was introduced into the abdomen prophylactically. In other cases, only in the presence of old infection was any sulfa-powder or crystals used.

Abdominal closure was made by layers; the peritoneum was closed by a continuous stitch of No. 0 or No. 1 plain catgut; the fascia was closed by a continuous stitch of No. 0 or No. 1 chromic catgut from each angle to the middle of the incision; the skin was closed with fine dermal interrupted vertical mattress sutures. No tension sutures were used (except in the case of 1 patient, because of obesity—weight 225 pounds—on whom an incidental incisional ventral herniorrhaphy was performed).

Spinal anesthesia was used in the majority of cases; cyclopropane and ether were used only when spinal anesthesia was refused. In a very few cases, the spinal anesthesia was supplemented with cyclopropane and ether near the close of the operation. One elderly patient, aged 74 years, was operated upon under local anesthesia of 1 per cent novocain for the removal of a very large ovarian cyst, a multilocular serous cystadenoma.

There were no postoperative dietary restrictions in either series. Diet was taken as tolerated, liquids, soft, or regular. Intravenous fluids were rarely administered immediately postoperatively, and this treatment was carried out only if the operation was extensive. Fluids were usually taken orally.

A retention catheter attached to a bottle was used after all plastic operations and vaginal hysterectomies. In the patients ambulated early,

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TABLE I.—EARLY AMBULATION

Type of operation	Pathology	No. cases
Total hysterectomy 5 cases	Fibromyomata uteri	2
	Highly malignant sarcoma of uterus	1
	Adenocarcinoma of uterus	1
	Uterine bleeding, cause unknown	1
*Subtotal hysterectomy 6 cases	Fibromyomata uteri	4
	Chronic pelvic inflammatory disease	2
Laparotomy 13 cases (Incidental appendectomy was done in 8 cases)	Simple cystic ovaries	4
	Bil. polycystic ovaries	1
	Multilocular serous cystadenoma of ovaries	2
	Rt. tubo-ovarian abscess and periappendicitis	1
	Retroverted uteri	3
	Scarred appendix and appendix vesiculosa	2
Vaginal hysterectomy and colpoperineoplasty 3 cases	Fibromyomata uteri with cystorectocele	1
	Prolapsus uteri (2–3°) with cystorectocele (1 patient had fibromyomata uteri)	2
Plastic operation 7 cases (Includes 1 urethroplasty and 1 Manchester operation)	Marked cystorectocele	4
	Marked cystorectocele following total hysterectomy	1
	Urethrocele and rectocele	1
	Prolapse (2°) of uterus with elongated cervix with cervicitis-cystorectocele	1
Combined abdominal and plastic operation 2 cases	Marked cystorectocele with 2 degrees prolapse and retroverted uterus	1
	Lacerated pelvic floor with chronic cervicitis and retroverted uterus	1
Low cervical cesarian section 1 case	Indication, 2 previous cesarian sections	1

*Unilateral or bilateral salpingo-oophorectomy or incidental appendectomy were performed on some of these patients.

TABLE II.—LATE AMBULATION

Type of operation	Pathology	No. cases
*Total hysterectomy 3 cases	Fibromyomata uteri	1
	Adenocarcinoma of uterus	1
	Uterine bleeding, cause unknown	1
*Subtotal hysterectomy 4 cases	Chronic pelvic inflammatory disease	1
	Uterine bleeding, cause unknown	1
	Endometriosis of ovary with uterine bleeding, cause unknown	1
	Adenocarcinoma of ovaries with adenomyosis uteri	1
Laparotomy 1 case	Bil. pyosalpinx.	1
Vaginal hysterectomy and colpoperineoplasty 4 cases	Prolapsus uteri 2–3 degrees with cystorectocele (one case of adenomyosis uteri)	3
	Complete procidentia uteri with marked cystorectocele	1
Plastic operation 5 cases (Includes 1 urethroplasty)	Marked cystorectocele (2 patients with elongated cervices with cervicitis requiring amputation)	4
	Urethrocele and rectocele	1

*Unilateral or bilateral salpingo-oophorectomy or incidental appendectomy were performed on some of these patients.

the catheter was kept in for the first 24 hours (except for 2 cases, one a vaginal hysterectomy performed on an obese patient weighing 217 pounds, and the other a urethroplasty in which the catheter was kept in for 48 hours). In the patients ambulated late, the retention catheter was used for 72 to 96 hours. In 3 total abdominal hysterectomies (2 in the early ambulated series and 1 in the late ambulated series) because some difficulty was encountered in the dissection of the bladder from the cervix, a retention catheter attached to a bottle was used for the first 24 hours. In all other cases patients were catheterized only when necessary.

A study of the patients treated revealed the following salient features:

The age range of the patients treated by early ambulation was from 15 to 74 years; of those treated by late ambulation 30 to 70 years. The mean age of those ambulated early was 41.2 years; of those ambulated late 52.1 years. The weight range of the patients ambulated early was 110 to 225 pounds; of the patients ambulated late 112 to 230 pounds. The nutritional status of the patients in both series was approximately the same.

In the early ambulation series, there were 2 patients with hypertensive heart disease, 1 with rheumatic heart disease, 2 with positive serology (Mazzini), and 1 with chronic bronchitis. In the late ambulation series there were 3 patients with hypertensive heart disease and 2 with diabetes mellitus.

Wound healing was not affected by the positive serology or the diabetes mellitus in either series.

The surgery performed on the patients ambulated early, included: 5 total abdominal hysterectomies; 6 subtotal hysterectomies; 13 laparotomies for surgery other than hysterectomy; 3 vaginal hysterectomies; 7 plastic operations; 2 combined abdominal and plastic operations; 1 cesarian section (this case is included because of the abdominal surgery entailed). For the pathology associated with these cases see Table I.

The surgery performed on the patients ambulated late, included: 3 total abdominal hysterectomies; 4 subtotal hysterectomies; 1 laparotomy for surgery other than hysterectomy; 4 vaginal hysterectomies; 5 plastic operations. For the pathology associated with these cases see Table II.

The patients who were ambulated early wore tight abdominal binders and, in the majority of instances, got up in a chair on the first postopera-

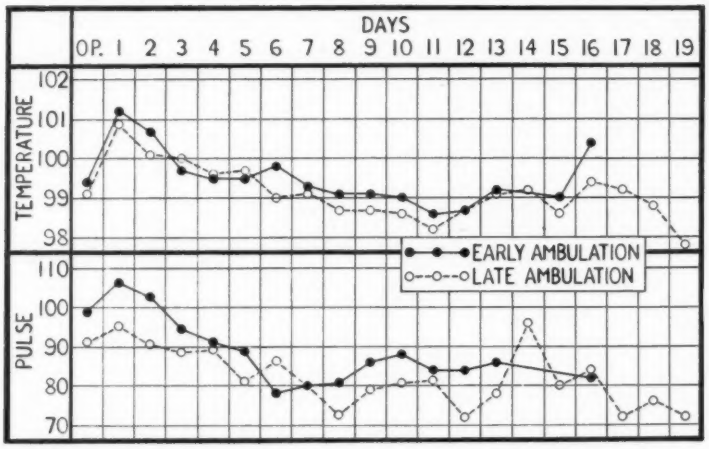

Fig. 1. A composite graph of the temperatures and pulse rates of both series.

tive day, with bathroom privileges. A few, because of hesitation and fear, dangled on the first day (8 out of 37 patients). All patients were up and about on the second day. Two patients who had undergone vaginal hysterectomies and 1 who had undergone a urethroplasty were ambulated on the second day because a retention catheter was used for the first 48 hours. Early ambulation was not insisted on but was encouraged. This series includes 4 patients, 2 of whom ambulated themselves on the third day, 2 of whom ambulated themselves on the fourth day. The majority of patients who were ambulated late got up in a chair on the seventh or eighth day; 1 patient got up on the sixth day, 1 on the tenth day, and 1 on the twelfth day.

A composite graph of the temperatures and pulse rates of both series (Fig. 1), such as was presented by Powers in his report, shows relatively little significant changes due to early ambulation. Like that of Powers, these were plotted by averaging the highest levels recorded for every patient on each day, and thus represent maximal elevations during the convalescent period.

Postoperative invalidism, both psychical and physical, was markedly reduced in the patients who were ambulated early. There was less apprehension on the part of the patient and the family, as to the patient's condition and prognosis. There was a notable decrease of the usual postoperative complaints on the part of the patient. Nursing care requirements were markedly reduced.

The necessity for catheterization of patients with abdominal surgery occurred for the most part on the operative day and the number of patients requiring catheterization was relatively the same in both series. Of the patients ambulated early, 7 of the 25 abdominal cases required catheterization and this on the operative day. One patient only required a second catheterization on the first postoperative day. Of those ambulated late, 3 of the 8 abdominal patients required catheterization and this was necessary on the operative day only.

All the patients on whom plastic operations and vaginal hysterectomies were done, whether ambulated early or late, showed the same relative frequency of catheterization following removal of the retention catheter. Of the patients ambulated early, 2 out of 12 required catheterization once; of the patients ambulated late, 1 out of 9 required catheterization once. The early ambulated patients, however, emptied their bladders more completely, suggesting that in these types of operation there was an earlier return of bladder tonicity with early ambulation. Although a study of residual urine was not carried out in all cases due to a shortage of nurses, the findings in the cases in which this study was done seemed to confirm this fact. A more complete study of all the cases, made by averaging the lowest quantities of urine voided, the highest quantities voided and the frequency of voiding for the first 3 days following removal of the retention catheter, revealed that the patients who were ambulated early voided larger quantities and less frequently (Table III).

In both series there were a few patients who were able to move their bowels without the aid of

an enema; however, the incidence was greater among those who were ambulated early (14 of the 37 patients ambulated early compared with 2 of the 17 patients ambulated late).

There were no cases of abdominal distention in the patients who were ambulated early and only 1 case of moderate distention in the patients who were ambulated late.

The requirements of sedation during the operative day were comparatively the same in both series. After early ambulation sedation was rarely required.

The number of hospital days here reported is not necessarily a true indication of the hospital days required for convalescence. Since patients came from many sections of the state and in many cases were required to travel great distances, discharge from the hospital was made according to the convenience of the patient and not necessarily at the time when the patient was physically able. Some patients stayed as long as 2 to 5 days beyond the time of discharge. Because this factor was constant in both series, the relative number of hospital days saved is still quite evident. The average number of hospital days required by the patients who were ambulated early was 8.72 days as compared with 13.94 days required by the patients who were ambulated late. Early ambulation, therefore, saved an average of 5.22 hospital days per case. A comparison of the average number of hospital days required according to the type of operation performed is given in Tables IV and V.

The patients ambulated early developed the following postoperative complications: unexplained fever, 2 cases; acute bronchitis, 1 case; phlebitis, 1 case; hematoma in incision, 1 case.

Unexplained fever occurred during the postoperative course of 2 patients, one upon whom a vaginal hysterectomy had been performed and the other a plastic operation. Physical examination and laboratory findings were negative in both cases.

Acute bronchitis occurred in a patient weighing 217 pounds, with known chronic bronchitis, on whom a vaginal hysterectomy was performed. The patient had a predisposing focus of infection and it is possible to conceive that early ambulation in this very obese patient prevented the possibility of bronchopneumonia.

Phlebitis occurred in a patient on whom a urethroplasty was performed. Early ambulation in this patient was evidently insufficient prophylaxis against this attack of phlebitis. It may be noted that this patient had a "milk-leg" in the opposite leg 20 years ago following a normal delivery.

TABLE III

Patients	Lowest quantity voided Ounces	Highest quantity voided Ounces	Frequency per day
Ambulated early	5 (150 c.c.)	13 (390 c.c.)	4
Ambulated late	4 (120 c.c.)	10 (300 c.c.)	6

A hematoma in an incision occurred in a patient who had a Gilliam suspension. The hematoma was at the level where the round ligaments were anchored to the fascia and evidenced itself by a 1-inch gape of the incision on the sixth postoperative day. While this hematoma may be attributed to early ambulation, it is conceivable that a small unrecognized bleeder may have been produced at the time of operation in one of the perforations of the fascia and recti muscles through which the round ligaments were drawn.

The patients ambulated late developed only 1 postoperative complication: 1 case of unexplained fever. Unexplained fever occurred after operation in a patient who had undergone a vaginal hysterectomy. Physical examination and laboratory findings were negative.

The "follow-up" on these patients revealed that the convalescent period at home was much less for those patients who were ambulated early. Of the patients ambulated early, 8 were able to resume their normal activities immediately after leaving the hospital; of those who were ambulated late only 1 was able to do so. The average convalescent period at home required by the patients who were ambulated early was 3.87 weeks, compared with 6.5 weeks required by those who were ambulated late. The average total convalescent period required by those who were ambulated early was therefore 3.3 weeks less than that required by those ambulated late. The duration of convalescence according to type of operation is shown in Tables IV and V.

A "follow-up" of both series, over a period of 6 to 8 months, has revealed no disruption of wounds, no incisional ventral hernias, no recurrent cystorectoceles, no prolapse of the vault of the vagina following vaginal hysterectomies.

DISCUSSION

The above data reveal certain obvious clinical advantages in early postoperative ambulation. A study of the etiology and pathology of postoperative pneumonia, atelectasis, embolism, infarcts, phlebothrombosis, etc., indicates that early ambulation also offers advantages in the prophylaxis of these conditions.

With the patient on her back following surgery, the stage is set for many hours of recumbency with

TABLE IV.—EARLY AMBULATION

Type of operation	†Hospital days (Average) Days	Convalescent period at home (Average) Days	Total convalescent period Days
*Total hysterectomy	9.8	29.4 (4.2 weeks)	39.2 (5.6 weeks)
*Subtotal hysterectomy	8.6	28 (4 weeks)	36.6 (5.22 weeks)
Laparotomies	7.2	15.26 (2.18 weeks)	22.47 (3.21 weeks)
Vaginal hysterectomy and colpoperineoplasty	10	51.31 (7.33 weeks)	61.31 (8.75 weeks)
**Plastic operations	9	35. (5. weeks)	44. (6.28 weeks)
Combined abdominal and plastic operations	9.5	28. (4. weeks)	37.5 (5.35 weeks)
Low cervical cesarian section	9	35. (5. weeks)	44. (6.28 weeks)
All types averaged in toto	8.72	27.09 (3.87 weeks)	35.81-(5.1 weeks)

*Unilateral or bilateral salpingo-oophorectomy or incidental appendectomy were performed on some of these cases.
†Number of hospital days recorded are not necessarily the actual number of hospital days required—frequent home transportation difficulty.
**1 case, complicated, requiring 23 days is not averaged.

shallow breathing (4, 25). There is a pooling of the tracheobronchial secretions in the finer ramifications of the bronchial tree and very often a disinclination to cough due to pain. This, in association with the limitation of the respiratory excursions, allows for an obstruction in the distal bronchioles. The free drainage by which the lung is kept in an aseptic condition is interfered with; the air distal to the obstruction is absorbed; the corresponding lobules collapse and in the occluded area, with a predisposing infection, a mild pneumonia may develop.

The increased lung expansion afforded by the exercise of early ambulation would no doubt aid in the prevention of the pooling and stasis of the tracheobronchial secretions, and hence early ambulation should be definite prophylaxis against such pulmonary complications.

The metabolism (7) and muscle tone of the recumbent patient are low. There is a decrease in the volume of flow in all the vessels of the body. The venous pressure is low, and the caliber of the veins, especially in the abdomen, pelvis, and legs, is much smaller than when sitting up. Only when the patient is sitting or standing are these veins constantly dilated. Frykholm suggested that collapsed veins may have endothelial damage, predisposing to later thrombosis. Veins, which are compressed and empty, due to pressure of the legs against the bed as suggested by Dock, may easily suffer endothelial damage and begin to thrombose while nearly empty. Dock further pointed out that phlebothrombosis may begin in the venules of the muscles and subcutis, or in the pelvic venous plexuses where complete stasis is possible. The formation of large clots propagated far along the system is made possible by prolonged recumbency. The dislodgment of clots with the formation of emboli is effected when after this prolonged recumbency there is a sudden rise of venous pressure such as is produced by getting out of bed or straining on a bed pan.

Pulmonary embolism has always been a bugbear of surgery, especially in gynecology and

TABLE V.—LATE AMBULATION

Type of operation	†Hospital days (Average) Days	Convalescent period at home (Average) Days	Total convalescent period Days
*Total hysterectomy	15.	74.62 (10.66 weeks)	89.62 (12.8 weeks)
*Subtotal hysterectomy	13.7	**	**
Laparotomies	21.	28. (4. weeks)	49. (7. weeks)
Vaginal hysterectomies and colpoperineoplasty	13.25	60.62 (8.66 weeks)	73.87 (10.55 weeks)
Plastic operations	12.6	36.4 (5.2 weeks)	49.0 (7. weeks)
All types averaged in toto	13.94	45.5 (6.5 weeks)	59.44 (8.49 weeks)

*Unilateral or bilateral salpingo-oophorectomy or incidental appendectomy were done in some of these cases.
†Number of hospital days recorded are not necessarily the actual number of hospital days required—frequent home transportation difficulty.
**Of 4 cases—1 reported immediate assumption of usual activities; 1 failed to report; 1 was fully active at the end of 2 weeks and 1 with bilateral adenocarcinoma of ovaries with metastases was still an invalid at 7 months. Therefore, the average convalescence would not give a true relative average for the period of convalescence for that type of surgery.

obstetrics. It may occur suddenly in uncomplicated cases of patients who have progressed satisfactorily. The patient is allowed up out of bed for the first time on the seventh day or later and like a bolt out of the blue, a fatal embolism occurs. Fortunately, this accident is not very frequent; however, when it does occur it is grim tragedy.

Since muscular activity increases the venous circulation of the lower extremities, walking would prevent stasis in the venules of the muscles; also, since sitting or standing increases the caliber of the pelvic veins, stasis in the pelvic vessels associated with recumbency is thus removed. The prophylaxis afforded by early postoperative ambulation against such postoperative accidents should be quite apparent.

Early postoperative ambulation in plastic operations and vaginal hysterectomies causes no additional pain or discomfort. Patients who were ambulated early felt much more comfortable and invalidism was greatly decreased. Pain on sitting in a chair is avoided by the use of an inflated rubber cushion ring.

There may be some pain in the incisional area of abdominal operations on the initial attempt to arise, but this quickly subsides. The patients then feel more comfortable and from then on they have very few, if any, complaints about pain. Patients who had previous laparotomies in which they had been treated by the conservative regimen of late ambulation, themselves volunteered the information that with early ambulation they had less discomfort and very little pain.

It has already been stated that a "follow-up" of the patients treated by early postoperative ambulation in this report, has revealed no wound disruptions, no incisional ventral hernias, no recurrent cystorectoceles, no prolapse of the vault of the vagina following vaginal hysterectomies; and a study of the etiology of these conditions suggests no reason why early postoperative ambulation should result in a greater incidence of these conditions.

The breakdown of plastic operations or the prolapse of the vault of the vagina following vaginal hysterectomies may be entirely attributed to poor surgery or poor tissue, fascia, etc. or both. Recurrent cystoceles or prolapse of the vault of the vagina following vaginal hysterectomies are seen frequently in patients who were ambulated late. Anatomically, it is not conceivable that walking or sitting produces any significant stress or strain on the fascial supports of the bladder or rectum, or the uterosacral and round ligaments which are used to support the vault of the vagina following vaginal hysterectomies. A cough or a sneeze in bed would cause more strain by the increased intra-abdominal pressure, thereby produced, than would walking or sitting.

R. A. Cutting wisely stated that "if unusual strains were a frequent cause of wound rupture, the condition might well be expected to occur with a far greater degree of frequency than it does, because even though unusual strain be construed rather narrowly, such strains occur far more frequently than wound rupture."

Brettauer, in 1899, was the first to describe wound disruption in the American literature, with a report of 3 cases. Several large series (3, 8, 10, 11, 12, 21, 24, 28, 29) have since then been reported. One is impressed with the variety of opinions as to etiology. There are many predisposing and precipitating factors suggested as being responsible for wound disruption.

The salient predisposing causes as evidenced by the many reports in the literature include the following: obesity or asthenia (28); malnutrition (28); hypoproteinemia (13, 15, 26, 28, 30); avitaminosis (13, 28); low ascorbic acid level (13, 28, 32); dehydration (28); diabetes mellitus and similar disturbances of sugar metabolism (32); malignancy (28) especially if previous radiation has been given, and presence of acute or chronic pelvic inflammation (28).

The technique of wound closure is of obvious importance and various factors have been emphasized. Many have stressed in the technique of wound closure the significance with respect to the careless hemostasis (14, 16), too tight suture of the fascia (6), the grasping of large masses of tissue in ligatures (18), excessive use of catgut (1), etc.

The salient precipitating factors, as evidenced by the many studies of evisceration, are all conditions which increase the intra-abdominal pressure (11, 12, 24, 28, 29). These include: abdominal distention, with severe coughing or persistent emesis, hiccoughing, etc.

The etiology (6, 18, 19) of postoperative incisional ventral hernia is similar to that of wound disruption. Here, too, poor operative technique and postoperative complications, such as abdominal distention associated with vomiting, coughing, and hiccoughing, are stressed.

Considering all these factors, it is difficult to conceive that wound disruption or incisional hernia should occur more frequently with early postoperative ambulation than those treated by late ambulation. Predisposing causes of wound disruption or incisional ventral hernia such as malnutrition, hypoproteinemia, avitaminosis,

scurvy (low ascorbic acid level), dehydration and so on should be eliminated by good preoperative care, a recognized necessity for all surgery. The importance of good operative technique in abdominal closure is taken for granted whether the patient is ambulated early or late. Should abdominal distention occur as a postoperative complication, the surgeon's judgment should of necessity forbid the continuation of early postoperative ambulation, if already instituted, and appropriate measures should be taken to treat the cause of the distention.

It is interesting to note that in many reports in the literature, the incidence of wound disruption appears to be approximately the same as the incidence of fatal pulmonary embolism following surgery. In a study of wound disruption, Schmitz and Beaton found an incidence of 0.18 per cent, Glenn and Moore (10), 0.66 per cent; Norris, 0.5 per cent; Singleton and Blocker, 0.67 per cent. Barker *et al.*, in a statistical study of pulmonary embolism, found that the incidence of fatal pulmonary emboli, associated with major gynecological surgery, ranged from 0.53 to 0.73 per cent. The mortality rate of wound disruption, however, appears to be at least 50 per cent less than that of pulmonary embolism. Bowen found that the mortality rate of wound disruption ranged from 16 to 75 per cent. The average reported mortality rate of wound disruption according to Schmitz and Beaton is 34.8 per cent. It seems logical, therefore, to employ early postoperative ambulation as prophylaxis against pulmonary embolism in spite of fear of wound disruption, which is unwarranted, as has been indicated.

SUMMARY

Fifty-four consecutive cases are reported; the first 17 cases were maintained on the conservative regimen of late ambulation, the following 37 cases in the group received early postoperative ambulation.

1. The temperature and pulse rates showed relatively little significant change due to early ambulation.

2. Postoperative invalidism, both psychical and physical, was markedly reduced in those patients ambulated early.

3. The nursing care requirements were markedly reduced.

4. No significant difference was noted in the requirements of postoperative catheterization in abdominal cases. In plastic operations and vaginal hysterectomies, however, an earlier return of bladder tonicity was suggestive in those patients ambulated early.

5. Those patients ambulated early were relatively more able to move their bowels without the aid of an enema.

6. Sedation was rarely required after patients were ambulated early.

7. The average number of hospital days required by the patients ambulated early was 8.72 days, by those ambulated late 13.94 days; thus saving an average of 5.22 hospital days per patient for those who were ambulated early.

8. The average convalescent period at home required by the patients ambulated early was 3.87 weeks; by those ambulated late 6.5 weeks. The average total convalescent period required by those who were ambulated early was 3.3 weeks less than that required by those ambulated late.

9. A study of the etiology and pathology of postoperative pneumonia, atelectasis, phlebothrombosis, embolism, and infarcts indicates that early postoperative ambulation also offers advantages in prophylaxis.

10. Pain and discomfort as a result of early postoperative ambulation were not in evidence in this series. In fact, the patients who were ambulated early had less pain and discomfort than those who were ambulated late.

11. Early postoperative ambulation in plastic operations and vaginal hysterectomies should result in no greater incidence of recurrent cystoceles or prolapse of the vaginal vaults following vaginal hysterectomies. Anatomically, there is no evidence of added significant stress on the fascial and ligamentous supports from early ambulation.

12. A study of wound disruption and incisional hernia suggests that early postoperative ambulation should not in itself result in a greater incidence of wound disruption and incisional hernia providing, of course, the patient has received good preoperative care and the usual good operative technique.

13. Follow-up in this series revealed no wound disruptions, no incisional hernias, no recurrent cystorectoceles, and no prolapse of the vaginal vaults following vaginal hysterectomies.

CONCLUSIONS

Early postoperative ambulation in gynecology reduces the usual postoperative invalidism, both psychically and physically, and results in a more rapid convalescence. Gastrointestinal and bladder tonicity may be increased. Very little, if any, sedation is required after early ambulation is instituted. Nursing care is markedly reduced. There is an increased economy for the patient.

There is a definite advantage in early ambulation as prophylaxis against postoperative pneu-

monia, atelectasis, phlebothrombosis, embolism, and infarcts. Early postoperative ambulation *per se*, should in no way increase the incidence of wound disruption, postoperative incisional hernia, recurrent cystorectoceles following plastic operation, or prolapse of the vaginal vault following vaginal hysterectomies.

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EDITORIAL

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IPSILATERAL SPASTIC RECTUS ABDOMINIS IN A PURELY THORACIC WOUND

OBSERVATIONS on wounds of the thorax within the first few hours after injury have yielded some interesting side lights on these dangerous wounds. In one action resulting in 250 deaths on the battlefield, 60 deaths or approximately 25 per cent were due to wounds involving mainly the chest. Death from chest wounds on the battlefield or at the forward dressing station occurs most frequently due to massive hemorrhage from injuries to the heart, the aorta, the vena cava, the hilar vessels, or even to the subclavian vessels running over the apex of the lung. If the wounded man survives the threat of immediate hemorrhage and can be transported to an evacuation hospital, his chances for survival are greatly increased, but even here death from exsanguination may still occur, although in decreasing numbers as pooled universal group O blood and massive transfusions are made as readily available as plasma.

A second cause of early death is a tension pneumothorax incident to a laceration of the lung or of a bronchus, which may open as the lung relaxes in expiration. The obvious dyspnea, the immobile but distended hemithorax, the resonance on percussion, and absence of breath sounds, give clearcut evidence of the need for prompt withdrawal of air, but not infrequently the need for the *continuous* escape of air is unrecognized, and death from respiratory and circulatory failure occurs. A patient, who has had one aspiration for a tension pneumothorax with removal of apparently sufficient air to correct the mediastinal displacement, must be under careful and repeated observation for the next 48 hours lest a recurrence of the pneumothorax be overlooked. The introduction of a needle or of a catheter into the chest for the continuous escape of air should not be approached with timidity even by surgeons inexperienced in thoracic work. If an underwater seal, or a flutter valve is also provided, one need have no hesitancy in producing such a temporary opening into the thoracic cavity.

A fascinating but poorly understood early observation in connection with wounds limited to the chest has been an accompanying abdominal wall rigidity, usually unilateral, occasionally bilateral, and often associated with subcostal tenderness on palpation and percussion, strongly suggesting an intra-abdominal injury. There is also absence or markedly reduced amplitude of excursion of the abdominal wall during respiration, suggesting an immobile or spastic diaphragm or even an

underlying peritonitis. Frequently these signs are present only in the early hours after injury, they disappear spontaneously, sometimes within 18 hours, and they rarely persist more than 48 to 72 hours. In the first few hours after injury they may be so pronounced that one might easily be tempted to perform an abdominal exploration for a ruptured viscus.

Occasionally, in association with through-and-through wounds of the lower right chest, the right diaphragm and dome of the liver may sustain an injury which is quite unsuspected before its disclosure at operation or at autopsy, with a resulting rigidity of the abdominal wall and tenderness of the entire abdomen due to the irritating effect of bile and blood in the peritoneal cavity.

It is not uncommon, of course, to find such abdominal spasticity and subcostal tenderness on the same side as a lower lobe pneumonia, attributable to involvement of the diaphragmatic pleura in the inflammatory process. In the cases under discussion there was no injury to the diaphragm and no inflammation except that incident to blood in the pleural space. In one case autopsy served to illustrate the frequently observed phenomenon of a spastic abdomen associated with injuries entirely limited to the chest.

A number of nonfatal cases could be cited illustrating the effect upon the abdominal wall of purely thoracic injuries. Conversely, similar phenomena involving the uninjured chest, consecutive to wounds of the abdomen have also been ovserved. What operator has not noted, following a McBurney incision, or a right rectus incision, or a wound of the flank, a definite lag in respiration, a limitation in the excursions of the chest, and diminished breath sounds on the side of the wound, even with no evidence of bronchial obstruction or atelectasis to explain it?

In one instructive instance, three observers independently concluded that a private with a large left flank wound draining feces through a tangential laceration of the colon, had a left subphrenic abscess due to high fever, diminished respirations, faint breath sounds, dullness suggesting a high diaphragm, and tenderness on heavy percussion of the left lower chest. When no pus was found on aspiration at several points, the wound itself was widely opened, and a large piece of shrapnel and sequestrated bone were removed from a lumbar abscess, followed by complete disappearance of all chest signs.

A connecting link between the two serous lined cavities is the sympathetic chain, but the mechanism whereby it acts is unknown due to our limited knowledge of the sympathetic pathways, and the direction of their impulses. The intercostal nerves may be part of a reflex arc capable of mediating painful stimuli from the site of injury and affecting the abdominal wall innervated by them. A third possible explanation lies in the irritating effect of free blood in the pleural space upon the parietal and diaphragmatic pleura and upon structures which are unaccustomed to its presence. The early disappearance of this effect may be the result of dilution of the blood through pleural weeping. Whatever its explanation, this highly interesting reciprocal relationship between the two major serous lined cavities of the body, and how it is mediated, should yield to carefully planned experimentation.

Surgeons generally should be aware that in the presence of a chest wound, a spastic tender abdomen does not necessarily require a laparotomy, and if clinical and x-ray studies definitely disclose that the missile in its line of flight did not traverse the abdomen or its parietes one may safely disregard the abdominal signs.

EMILE HOLMAN.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE book by Clement A. Smith, *The Physiology of the Newborn Infant*,[1] is a monograph which deserves more than passing notice. Pediatricians and obstetricians particularly will find it useful. Lack of a source book of information on this subject has long been felt. New clinical observations and scientific research during the last few years have added much to knowledge in this field and have made all previous accounts of neonatal physiology obsolete. The present text assembles these data.

The text concerns itself with the period of the newborn and its transition from fetal life. The subjects of respiration, circulation, blood, metabolism, digestion, assimilation, renal physiology, endocrinology and immunology are treated. Thus it is quite a complete treatise of neonatal physiology with the exception of the nervous system and sense organs. The author states that the absence of the section devoted to the nervous system is not an oversight; most of the available knowledge upon that subject, he points out, is limited to the fetus or is anatomical in nature or considers the newborn period only briefly in relationship to general neuromuscular development. It is indeed true that physiology of the nervous system at the time of birth and during the first few months of life is a *terra incognita*.

The author himself has contributed scientifically to a number of the subjects dealt with in his book. Thus, he writes with great insight. The reviewer was especially pleased with the chapters on respiration and circulation. However, each succeeding chapter of the book is so full of new and important information that it seems more important than the preceding one. None is dull; each makes good reading.

One of the outstanding features of Professor Smith's monograph is the presentation at the conclusion of each chapter of a clinical summary in which the scientific data are discussed briefly from the standpoint of practical medicine. It is these summaries which make the book so useful to the clinical reader. Another interesting summary is found in a table printed on the back inside cover. This is a table of normal values at birth and on succeeding days thereafter. It serves as a ready and handy reference synopsis. Excellent bibliographies appear at the end of each chapter.

The Physiology of the Newborn Infant is very attractively printed and bound. It is not a large book. The text including the index occupies only 312 pages. Great credit is due the author for getting into such small volume so very much useful and interesting material: WILLIAM F. WINDLE.

[1] THE PHYSIOLOGY OF THE NEWBORN INFANT. By Clement A. Smith, M.D. Springfield, Illinois: Charles C Thomas 1945.

THE third edition of *Fractures of the Jaws* by Ivy and Curtis[2], will be received with proper appreciation by all who have to deal with maxillofacial surgery. The writing is clear and concise, and the subject matter carries the authority based on years of personal experience. The authors describe their own successful methods and also those of contemporaries in a generous manner. The character of the text remains the same; however, various new techniques and methods of fixation have been added.

We would particularly draw attention to the sections on roentgenographic technique and dietary management. These two important adjuncts to the successful treatment of jaw fractures cannot be too highly commended. Proper attention to these precepts will facilitate reduction of the fracture and recovery of the patient.

This compact book is well and profusely illustrated and it is a pleasure to suggest that every dentist, maxillofacial and general surgeon would profit by adding it to his library to read, study, and have available for ready reference.

FREDERICK W. MERRIFIELD.

THE *Primer of Electrocardiography*[3] by George Burch, M.D., and Travis Winsor, M.D. describes in detail the fundamentals of electrocardiography. In the strict sense, the title is somewhat misleading for the book goes into more detail than the word "primer" would lead one to believe. On the other hand, the authors probably felt that this was apropos inasmuch as only the basic considerations of this diagnostic procedure were covered. Through the liberal use of diagrams, each point is adequately exemplified. The theories of electrocardiography, precardial leads, and diseases of the heart beat are well covered. The chapter on the clinical significance of the various components of the electrocardiogram is well written and will be of definite value to the beginner. It will also serve as a handy reference to those who are more thoroughly versed in electrocardiography, as it contains many details which cannot be found in books stressing interpretation. Although no photographs of actual electrocardiograms are included, the important

[2] FRACTURES OF THE JAWS. By Robert H. Ivy, M.D., D.D.S., F.A.C.S., and Lawrence Curtis, A.B., M.D., D.D.S., F.A.C.S. 3d ed. Philadelphia: Lea & Febiger, 1945.

[3] A PRIMER OF ELECTROCARDIOGRAPHY. By George Burch, M.D., F.A.C.P., and Travis Winsor, M.D. Philadelphia: Lea & Febiger, 1945.

changes occurring in various types of heart abnormalities are adequately demonstrated. When used in conjunction with a manual stressing interpretation, it should prove helpful in the study of electrocardiography. T. R. VAN DELLEN.

THE second edition of a very clear and practical book on *The Intervertebral Disc*[1] by Bradford and Spurling brings up to date our knowledge of this subject and places special emphasis on the clinical and neurological diagnosis of herniation of these discs. Growth and mechanical factors are discussed in the first chapter, with emphasis on the great anterior hydraulic compressive force placed upon the nucleus pulposus of the fourth and fifth lumbar discs in forward lifting strain. Pathology associated with age change is considered an important factor in disc herniation, although sclerosis, narrowing and vertebral hypertrophic changes are not commonly related to nucleus pulposus herniation.

The clinical study of patients with "low back and sciatic pain" is very well presented except that there is continued confusion in reference to pain or "sciatica" "along the course of the great sciatic nerve" and lack of clear definition of symptoms and signs of single nerve root distribution. It is regrettable that these authors, who have been leaders in emphasis of neurologic diagnosis and unnecessary use of the spinogram, should be unable to present any consistent dermatome pattern in the lower extremity and continue to use the somewhat unauthoritative Tilney and Riley for illustrations of dermatome patterns. These charts were taken from Dejerine (1914) without any very evident original work to support them, and certainly are outdated by the more authoritative work of Foerster (1933). The irregularity of the areas of hypesthesia in clinical cases illustrated in this book denotes inaccuracy of technique in plotting these areas. Also there are conflicting statements about the occurrence of sensory loss in association with single nerve root involvement, the authors tending to adhere to Foerster's dictum that this does not occur, but citing a high percentage (75 per cent) of detectable hypesthesia in proved herniated nucleus pulposus cases with admitted single nerve root involvement. Better technique is needed on this subject, as others are able to outline consistent diagnostic areas of dermatome hypalgesia from unquestionable single nerve root loss.

The roentgenological presentation calls attention to the usual lack of diagnostic findings of herniation of the nucleus pulposus except by myelography or spinogram. The authors very properly reserve the use of the spinogram to atypical or doubtful cases in which localization cannot be made by history and neurologic signs, calling attention to the possible complications and uncertainties of intraspinal foreign media.

[1] THE INTERVERTEBRAL DISC, WITH SPECIAL REFERENCE TO RUPTURE OF THE ANNULUS FIBROSUS WITH HERNIATION OF THE NUCLEUS PULPOSUS. By F. Keith Bradford, M.D., and R. Glen Spurling, M.D. 2d ed. Springfield, Illinois: Charles C Thomas, 1945.

Distinction is made in the application of manipulation therapy, it often being beneficial in early cases with predominant midline low back pain, but liable to do harm in longer continued cases with entirely lateralized nerve root pain indicative of unreducible nucleus herniation. These latter cases may improve under long continued conservative rest or orthopedic treatment, due to subsidence of acute swelling or to a destroyed insensitive nerve root. Surgical treatment by very limited hemilaminectomy carries less than 1 per cent risk, does not significantly weaken the supporting structure of the back, and offers immediate relief of the lateralized nerve root pain. A more conservative attitude is held when low back pain predominates, as spinal fusion then may be necessary. Single nerve root section may be done to free a nerve from fibrotic adhesions and leaves no disabling functional loss.

The final discussion is interesting in the critical analysis of other reports. The authors consider "it now well established that total involvement of either the 5th lumbar or 1st sacral nerve will usually produce objective sensory changes," contrary to Foerster's dictum, while on a later page they state "involvement of only one nerve does not often produce hypesthesia." Dandy's contributions on "concealed discs" and "surgical excision of discs" are considered not well founded. Primary sciatic neuritis and sacroiliac strain are called clinical curiosities. Kellgren's dermatome pattern of referred pain from interspinous ligament injection is commended for its dermatome localization but on the preceding page the authors state that "localized pain—is not very reliable in identifying the roots involved" by herniation of nucleus pulposus. The orthopedic idea that narrowing of the 5th lumbar intervertebral foramen commonly causes nerve root pain is negatived by the usual finding of a herniated nucleus pulposus compressing the 5th nerve root when symptoms of this root involvement are present. It is stated that "there can be no doubt that the incidence of anomalies is greater in a series of patients complaining of low back and sciatic pain than in a control series," inasmuch as this condition seems to predispose to nucleus pulposus herniation, although in itself does not cause nerve root symptoms.

Cervical herniations are presented somewhat briefly, but with emphasis on the recent establishment of small lateral herniation in the lower cervical region as a common cause of pain radiating from the neck over the shoulder and into the arm and hand, with subjective sensation of paresthesia or numbness. As in the leg the pain and numbness follow a compressed single nerve root distribution and hypesthesia or hypalgesia may be demonstrated. Surgical relief can be given, as in the lumbar herniation, after trial of conservative measures. Occasionally wide herniation of annulus as well as nucleus will cause cord or cauda equina compression and demands prompt relief by surgical procedure.

J. JAY KEEGAN.

THE author of *Acute Injuries of the Head*[1] is one of the leading neurosurgeons of England. By training, surgical background, and large personal experience in the field of craniocerebral injuries he is thoroughly qualified to write on the subject of head injuries.

The book is addressed to the general practitioner and the general surgeon, whom the author regards as "vital links" in the care of patients with cranial injuries. The subject of craniocerebral injuries has been covered from every angle in this book. The chapters on the mechanisms of injury and pathology are splendid. Those portions of the book describing technical procedures and operations are clearly written and generously illustrated. Posttraumatic sequelae are thoroughly dealt with. The author has given very thoughtful, realistic discussion of the organic and the functional factors contributing to the typical postconcussion syndrome with helpful guides for expressing the relative rôle played by these two factors in any patient. Principles of treatment described in the book will have the approval of most neurosurgeons. This reviewer differs with the author's opinion regarding the value of subtemporal decompression and repeated spinal drainage in the treatment of closed head injuries, but it must be recognized that these are still unsettled issues. The author's style of writing is pleasing and invites further reading. He tends to avoid generalizations and prefers to make his points by numerous well chosen illustrative case records.

If any criticism were to be made of the book it would be in regard to the arrangement of subject matter. The book might be improved a bit, in the reviewer's opinion, by a change of certain chapter headings; for instance, Chapter III, which is titled "Diagnosis" might better be titled "Clinical Manifestations and Typical Clinical Syndromes." Again, the arrangement of subject matter might be improved in one or two places; for instance, the chapter on pathology deals only with pathology of cerebral injuries, whereas the pathology of cranial fractures is dealt with in a subsequent part of the book, describing the treatment of these fractures. At another place in the book, under the subject heading of "Spinal Puncture," the author digresses far enough to discuss treatment of primary shock, transfusion, the management of associated visceral wounds, and the excision of compound fractures. At another place, in the midst of a chapter on diagnosis, the author consumes one full page in discussing the indications for subtemporal decompression. The discussion itself is entirely proper, but the place in which the author has introduced it in the book appears to me untimely.

These are, of course, minor considerations judged against the general excellence of the subject matter and can be corrected in subsequent editions. The book is of comfortable size and pleasant to handle. Paper and printing are good. Illustrations are numerous and excellent. The author, in his preface to the second edition, says, "I believe that any general practitioner will find perusal of this book not only valuable, but will find the subject interesting, and even exciting." With that opinion, I concur.

JOHN E. SCARFF.

[1] ACUTE INJURIES OF THE HEAD; THEIR DIAGNOSIS, TREATMENT, COMPLICATIONS AND SEQUELS. By G. F. Rowbotham, B.Sc. (Manch.), F.R.C.S. (Eng.). Foreword by Norman M. Dott, M.B. Baltimore, Md.: Williams & Wilkins & Co., 1945.

THE fourth edition of Kuntz' *A Textbook of Neuroanatomy*[2] follows the traditional pattern of introducing the gross topography of the nervous system with comparative and embryological sections, then of reviewing the histology of nervous tissue and proceeding from peripheral nerve into the spinal cord, to mount by several stages through the brain stem and emerge at the cerebral cortex. Within the limits imposed by such a regional approach, in which, for example, consecutive chapters are devoted to nuclear connections of the cranial nerves, the cerebellum, the diencephalon, the optic connections and the autonomic nervous system, the author presents a clear description of neuroanatomy, without excessive detail and with a concise summary at the end of each chapter. This last unusual feature will doubtless be greatly appreciated by the hard pressed medical student of today.

Passing reference to the functional and clinical significance of structures is made throughout the text and an entire chapter is devoted to that of the cerebral cortex. A laboratory guide is appended, together with a series of case histories illustrating the clinical aspects of injuries to the peripheral nerves, spinal cord, and brain. Because all the brain lesions resulted from vascular disturbances, the student may wonder why no reference to the blood supply of the nervous system was incorporated in the text.

H. W. MAGOUN.

IN the third edition of Kuntz' *The Autonomic Nervous System*,[3] presentation of the general anatomy and physiology is succeeded by detailed discussions of the innervation of each of the organs, visceral pain, histopathology, disease, and autonomic neurosurgery. Specific citation of original articles is a constant feature and the one hundred twenty pages of assembled references constitute a unique bibliography in the many aspects of this field.

In the preface, mention is made of the temptation to give undue weight to recent contributions that is resisted in varying degrees to preserve a balance between the new and the old. The reviewer is one who would like to have seen this resistance relaxed in the discussion of such topics as the terminal reticulum and ground plexus and the sympathetic innervation of skeletal muscle.

The book is recommended as a valuable reference work to everyone interested in the autonomic nervous system.

H. W. MAGOUN.

[2] A TEXTBOOK OF NEUROANATOMY. By Albert Kuntz, Ph.D., M.D. 4th ed. Philadelphia: Lea & Febiger, 1945.

[3] THE AUTONOMIC NERVOUS SYSTEM. By Albert Kuntz, Ph.D., M.D. 3d enl. rev. ed. Philadelphia: Lea & Febiger, 1945.

THE work described in *Pulmonary Tuberculosis in the Adult* by Max Pinner[1] is a welcome addition to the tuberculosis literature. The material has been wisely selected from the welter of divergent viewpoints and connected, or really molded, into a unit that is clearly presented, easy to read and understand, and one that compels an absorbing interest in the subject.

Doctor Pinner states in the preface that he does not pretend to have written a textbook or a guide to treatment or diagnosis, but aims more to stimulate interest in the form of an introduction to the dynamic process of tuberculosis. His purpose has been fully realized. In addition to the many fascinating "essays" on the disease, the author has given a valuable collection of short abstracts of important articles on the various topics.

No worker in tuberculosis or chest diseases should be without this book, although the work does not have, nor pretend to have, anything but general usefulness for the surgeon.

The illustrations are adequate, properly chosen, and well reproduced. The type, printing, paper, and binding are worthy of the high standards already set by the publisher. HENRY C. SWEANY.

THE third revision by Stander of *Textbook of Obstetrics*[2], represents the ninth edition of *Williams' Obstetrics*, but it is published under the present author's name since, as he states in the preface, it embodies his teaching and practice and therefore he assumes full responsibility.

This volume consists of 1200 pages of subject matter with over 700 well chosen illustrations. The first 500 pages deal with the anatomy of the female pelvis, physiology, development of the fetus and changes occurring therewith, endocrine function and their practical applications in obstetrics, and the conduct of pregnancy and labor. An excellent review of the subject of analgesia and anesthesia is included. The following 700 pages are devoted to the pathology of pregnancy, labor, and the puerperium. Abnormal pelves and operative procedures are considered here. The sections on toxemias, extrauterine pregnancy, and abnormal pelves are particularly comprehensive and embody the latest contributions on these subjects. One important omission, however, is noted under the subject of contracted pelves, namely the Hillis impression method. All other methods for attempting to determine the relationship between the size of the fetal head and the maternal pelvis are described. The Hillis impression method, since it is the simplest and without the objection of vaginal manipulation, is by far the most practical and useful of all such maneuvers, and should, therefore, be included in all obstetrical textbooks.

Stander's third revision of *Williams' Obstetrics* brings it up to date with such recent advances as the importance of the Rh factor in obstetrics and the addition of penicillin and the sulfonamides to the obstetrician's armamentarium; but it also retains the simplicity of style and the clear, concise presentation of the subject that has characterized this text in previous editions. CHESTER C. DOHERTY.

THE volume entitled, *The Osseous System*,[3] is the fourth of a series of handbooks of roentgen diagnosis being published by the Year Book Publishers. As in previous volumes the material is so arranged that the illustrations are on the right hand page and the description and legends on the opposite side. The concise but lucid subject matter is illustrated by 432 figures on 148 plates all in the negative phase. Throughout the text, the author emphasizes the pitfalls of diagnosis and urges that the occasional radiographer always think of the maxim, "What might it be besides what I think it is?"

The contents of the volume is divided into five sections: technique: principles of interpretation: roentgen anatomy; injuries to the skeletal system other than the spine; the spine; bone diseases and abnormalities in childhood; bone diseases occurring principally in adult life. A short bibliography appears at the end of each section and an adequate index is appended.

This volume is a handy-sized, modestly priced atlas and can be recommended to general practitioners, surgeons, and internists as a diagnostic aid. It should be regarded, as indicated, as a primer rather than an encyclopedia. EARL E. BARTH.

THE author of *Electrotherapy and Light Therapy*[4] is an outstanding authority in the field of physical medicine. The fifth edition of this work offers a concise presentation of all present day phases of physical medicine with special emphasis on electrotherapy and light therapy. The newer uses and methods of electronics, electrodiagnosis, ion transfer, and ultraviolet radiation have all been incorporated. The chapter on exercise has been considerably enlarged and a new chapter on hypothermy has been added together with a revised glossary covering definitions of electrotherapy and light therapy, muscle and nerve action, and mechanotherapy. Each chapter has been brought up to date. New illustrations have been added and obsolete ones omitted. The illustrations are excellent.

One of the peculiar features of the book, which has enabled it to maintain a position of leadership for fifteen years, is the interesting manner in which the subject is presented. It contains much valuable information, and it is a safe guide to place in the hands of the practitioner. JOHN S. COULTER.

[1] PULMONARY TUBERCULOSIS IN THE ADULT; ITS FUNDAMENTAL ASPECTS. By Max Pinner, M.D. Springfield, Ill.: Charles C Thomas, 1945.

[2] TEXTBOOK OF OBSTETRICS; DESIGNED FOR THE USE OF STUDENTS AND PRACTITIONERS (formerly Williams' Obstetrics). By Henricus J. Stander, M.D., F.A.C.S. Stander's 3d rev. New York and London: D. Appleton-Century Co. Inc., 1945.

[3] THE OSSEOUS SYSTEM; A HANDBOOK OF ROENTGEN DIAGNOSIS. By Vincent W. Archer, M.D. Chicago: The Year Book Publishers, Inc., 1945.

[4] ELECTROTHERAPY AND LIGHT THERAPY; WITH THE ESSENTIALS OF HYDROTHERAPY AND MECHANOTHERAPY. By Richard Kovács, M.D. 5th rev. ed. Philadelphia: Lea & Febiger, 1945.

"THE subject of this book is physiology; not 'physiology from above' but 'physiology from below'; not physiology originating essentially to fill human needs and help suffering individuals, but physiology as a branch of physical chemical sciences dealing with life as a physical, though exceedingly complex system, that may be subjected to scientific analysis like any other natural object." Quotation is from the preface of *Physical Chemistry of Cells and Tissues*[1] by Rudolf Hoeber *et al.*

The reviewer is very much in sympathy with the aims of this book. American science, in general, is far too concerned with "practical applications." Nature is a lady who must be wooed for her own worth before she will reveal herself. Certainly, there is a tremendous need for such a book as we have here and a still greater need for people with the viewpoint of the authors of this excellent text. It is a book which must be bought by all who wish to understand what is now known about many important phases of life processes.

The first 91 pages were written by David I. Hitchcock and deal essentially with physical chemistry of solutions. He discusses diffusion in solution, reaction velocity, thermodynamics, electromotive force, osmotic pressure, electrokinetics and distribution coefficients. Hitchcock stays on broad and well trodden highways. This section is clearly written but parts of it are very scratchy and rather thin. For example, the reviewer doubts that a reader who is not already familiar with thermodynamics could profit very much by reading the chapter on this subject: too much territory is covered in the 12 pages. This brevity is carried to extreme in the discussion of dielectric constants, dipole moments and the Deby-Hueckel theory of strong electrolytes. Two pages are devoted to these subjects!

Section 2 which covers 120 pages was written by J. B. Bateman. In this section Bateman deals with molecular forces, determination of sizes and shapes of large molecules, hydration, protein structure, x-ray diffraction analysis, the structure of crystals and fibers and surface monolayers. There is much excellent material in this section. The part dealing with crystal structure is especially informative. Bateman covers many complex subjects and the reviewer appreciates the great difficulty of presenting these topics simply, but it must be said that this section suffers from a lack of clarity.

The strictly biological part of the book begins with Hoeber's section (141 pages) which deals with the penetration of cell membranes by organic nonelectrolytes, by electrolytes, by weak acids and bases, by dyestuffs, by water, and finally he considers the chemistry and physics of plasma membranes. He brings to these subjects more than 40 years of experience and he has performed a great service to all of us in summarizing with completeness and detail the existing knowledge about cell membranes. Hoeber follows the Collander and Baerlund "lipoid-sieve theory" of cell membranes. He discusses active and passive uptake of substances and describes how they can be distinguished from each other. One cannot help but have the feeling after reading this section that future progress in the study of cell penetration must involve a fuller consideration of the interior of cells. It appears that the penetration and action of narcotics is very obscure and would especially benefit by such expansion.

A section has been contributed by David R. Goddard (71 pages) on the respiration of cells and tissues. Goddard's section is simply written, clear and up-to-date. He deals with the rate of respiration as limited by the rate of diffusion of oxygen. The kinetics of activated reactions are discussed and after a short chapter on the nature of oxidation, he discusses respiratory enzymes. There follows a chapter on the relation between fermentation and respiration. Finally there is a chapter on the utilization of liberated energy. This last is by necessity very incomplete since our knowledge of this utilization is at the present exceedingly imperfect.

W. O. Fenn has 75 pages on contractile tissues with special reference to striated and smooth muscle. This is a well balanced and critical review of experiments and theories of muscle contraction. It appears from this review that there still remains much to be known about muscle contraction. Muscle physiology has passed through several phases until now it has become a sophisticated science and one has to have a background in several branches of science to appreciate all the modern developments. One can, however, note considerable recent progress and as Fenn writes, "At last the contractile machinery has become more than a structure which is passively acted upon by lactic acid or some other metabolic product. It is as if steam had at last been admitted to the previously empty cylinders of the muscle machine."

Hoeber concludes the book with a section (110 pages) on passive and active transfer in animal and plant tissues. In this section he deals with intestinal absorption, formation of urine, permeability of body surfaces of animals and plants, formation of digestive juices, and finally a discussion of some of the mechanisms which may be involved in active transfers. Here again as in the section on cell membranes there is a wealth of detail. HENRY B. BULL.

THE fourth edition of Christopher's *A Textbook of Surgery*,[2] an already well established standard text by eminent American authors, has been made an even more complete and currently correct basic volume for students and reference point for practitioners. This has been accomplished through the addition of sections devoted to recent military experiences as well as the modification of other sections on the basis of progress in both civilian and military surgery. In view of the earliness of publi-

[1] PHYSICAL CHEMISTRY OF CELLS AND TISSUES. By Rudolf Hoeber. With collaboration of D. I. Hitchcock, J. B. Bateman, D. R. Goddard, and W. O. Fenn. Philadelphia and Toronto: The Blakiston Co., 1945.

[2] A TEXTBOOK OF SURGERY. By American Authors. Edited by Frederick Christopher, B.S., M.D., F.A.C.S. 4th ed. Philadelphia and London: W. B. Saunders Co., 1945.

cation following the end of World War II, remarkably few statements will require considerable correction as a result of reports on military observations made available subsequent to completion of the present edition. This volume maintains the high standards of format and illustration which characterized previous editions of the work.

AMBROSE H. STORCK.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

TRATAMENTO CIRURGICO DO CANCER DA MAMA. By Alberto Francia Martins, M.D. Vol. 3, Nos. 9 and 10. Sao Paulo, Brazil: Revista de Medicina e Cirurgia de Sao Paulo, 1943.

TRATAMIENTO DE LAS ULCERAS PERFORADAS DEL ESTOMAGO Y DUODENO. By Julio A. Acebal, M.D. Rosario, Brazil: Libreria y Editorial Ruiz, 1945.

SURGICAL NURSING. By E. L. Eliason, A.B., M.D., Sc.D., F.A.C.S., L. Kraeer Ferguson, A.B., M.D., F.A.C.S., and Evelyn M. Farrand, R.N., B.S. 7th ed. Philadelphia: J. B. Lippincott Co., 1945.

TRANSACTIONS OF THE AMERICAN GYNECOLOGICAL SOCIETY. Edited by Howard C. Taylor, Jr., M.D. Vol. 68. St. Louis: The C. V. Mosby Co., 1945.

NITROUS OXIDE-OXYGEN ANESTHESIA; MCKESSON-CLEMENT VIEWPOINT AND TECHNIQUE. By F. W. Clement, Major, M.C.(A.U.S.). 2d ed. Philadelphia: Lea & Febiger, 1945.

THE EXTREMITIES. By Daniel P. Quiring, Ph.D., Beatrice A. Boyle, Erna L. Boroush, M.A., and Bernadine Lufkin, A.B. Philadelphia: Lea & Febiger, 1945.

ATLAS OF SURGICAL APPROACHES TO BONES AND JOINTS. By Toufick Nicola, M.D., F.A.C.S. Foreword by Norman T. Kirk, Major General, U.S. Army, The Surgeon General, New York: The Macmillan Co., 1945.

AN INTRODUCTION TO CLINICAL SURGERY. Surgical Wherefores and Therefores. A Reasoned Explanation of Surgical Note-Taking. By Charles F. M. Saint, C.B.E., M.D., M.S., F.R.C.S.(Eng.), F.R.A.C.S. Cape Town: The Post-Graduate Press by The African Bookman, 1945.

MEN WITHOUT GUNS. Text by DeWitt Mackenzie, War Analyst of The Associated Press, Descriptive Captions by Major Clarence Worden, Medical Department of the United States Army. Foreword by Major General Norman T. Kirk, Surgeon General of the United States Army. Illustrated with 137 Plates from the Abbott Collection of Paintings Owned By the United States Government. Philadelphia, Toronto: The Blakiston Co., 1945.

FRACTURAS—LUXAÇÕES TORCEDURAS. By Renato Da Costa Bomfim. São Paulo: E. G. Revista dos Tribunais Ltda., 1945.

INDUSTRIAL TOXICOLOGY. By Alice Hamilton, A.M., M.D., and Rutherford T. Johnstone, M.D. Edited by Henry A. Christian, A.M., M.D., LL.D., Sc.D.(Hon.), F.A.C.P., Hon. F.R.C.P.(Can.) Reprinted from Oxford Loose-Leaf Medicine. New York: Oxford Univ. Press, 1945.

GYNECOLOGIC NURSING. By Robert James Crossen, A.B., M.D., F.A.C.S., and Frances W. Hoffert, R.N., B.S. 3d ed. St. Louis: The C. V. Mosby Co., 1946.

SURGICAL TREATMENT OF THE MOTOR-SKELETAL SYSTEM. By Frederic W. Bancroft, A.B., M.D., F.A.C.S., and Clay Ray Murray, M.D., F.A.C.S. Parts 1 and 2. Philadelphia, London, Montreal: J. B. Lippincott Co., 1945.

BIOLOGICAL ACTIONS OF SEX HORMONES. By Harold Burrows, C.B.E., Ph.D., F.R.C.S. Cambridge: The University Press, 1945.

SYNOPSIS OF GYNECOLOGY. Based on the Textbook Diseases of Women. By Harry Sturgeon Crossen, M.D., F.A.C.S., and Robert James Crossen, M.D., F.A.C.S. 3d ed. St. Louis: The C. V. Mosby Co., 1946.

EL HOMBRE NUESTRO TEMA MORFOLOGICO. By Prof. Dr. Pedro Belou. Buenos Aires: La Semana Medica, 1945.

HOMEAJE AL PROFESOR PEDRO BELOU. Buenos Aires: Guillermo Kraft Ltda., 1941.

THE CHEMISTRY OF ANESTHESIA. By John Adriani, M.D. Springfield, Ill.: Charles C Thomas, 1946.

BRENTHURST PAPERS. Edited by Jack Penn, M.B.E., M.B.ChB., F.R.C.S.E. Johannesburg: Witwatersrand University Press, 1944.

THE PHYSIOLOGICAL BASIS OF MEDICAL PRACTICE. By Charles Herbert Best, C.B.E., M.A., M.D., D.Sc., F.R.A., F.R.C.P., and Norman Burke Taylor, V.C., M.D., F.R.S., F.R.C.S., F.R.C.P., M.R.C.S., L.R.C.P. Baltimore: The Williams & Wilkins Co., 1945.

ROENTGEN DIAGNOSIS OF DISEASES OF THE GASTRO-INTESTINAL TRACT. By John T. Farrell, Jr., M.D. Springfield, Ill.: Charles C Thomas, 1946.

IRISH MEDICAL DIRECTORY AND HOSPITAL YEAR-BOOK. 8th ed. Dublin: The Parkside Press Limited, 1945.

CLINICAL ELECTROCARDIOGRAPHY. By David Scherf, M.D., F.A.C.P., and Linn J. Boyd, M.D., F.A.C.P. Philadelphia: J. B. Lippincott Co., 1946.

NUTRITION AND CHEMICAL GROWTH IN CHILDHOOD. Vol. 2., Original Data. By Icie G. Macy, Ph.D., Sc.D. With a Foreword by Lawrence Reynolds, M.D., and a Supplement by Julia Outhouse Holmes, Ph.D. Springfield, Illinois: Charles C Thomas, 1946.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

W. EDWARD GALLIE, *President*
IRVIN ABELL, Louisville, *President-Elect*

Committee on Arrangements
HOWARD PATTERSON, *Chairman;* FRANK GLENN, *Secretary*

PRELIMINARY PROGRAM FOR 1946 CLINICAL CONGRESS NEW YORK, SEPTEMBER 9 TO 13, 1946

THE thirty-second Clinical Congress of the American College of Surgeons will be held in New York City at the Waldorf-Astoria from September 9 to 13. This will be the first Congress since the 1941 meeting in Boston. Between 1942 and 1945 the Congress was voluntarily cancelled each year in order to lessen the transportation difficulties and to conserve the time of medical and hospital personnel who were overburdened because of the absence of so many of their associates on duty with the armed forces. By autumn the majority of these will have returned and the time seems most auspicious for a great postwar Congress. The preliminary announcement of the plans has been received with enthusiasm by both the military and civilian groups.

CLINICAL PROGRAM

Under the leadership of a strong and representative Committee on Arrangements, plans are under way for a complete and varied program for the five day meeting. The hospitals and medical schools will co-operate in scheduling operative and nonoperative clinics and demonstrations.

COMMITTEE ON ARRANGEMENTS

Howard Patterson, *Chairman*
Frank Glenn, *Secretary*
Frank Adair
Albert H. Aldridge
Thomas M. Brennan
E. Jefferson Browder
George F. Cahill
Henry W. Cave
Ralph Colp
Edward J. Donovan
Merrill N. Foote
John H. Garlock
Charles A. Gordon
George J. Heuer
J. William Hinton
George H. Humphreys
William F. MacFee
John H. Mulholland
W. Barclay Parsons
Otto Pickhardt
Thomas H. Russell
Raymond P. Sullivan
Howard C. Taylor, Jr.
William Crawford White
Philip D. Wilson

Visiting surgeons will have ample opportunity to attend well arranged programs of many different kinds in several of the excellent hospitals in the Greater New York area. These programs will include general and special demonstrations such as fractures, cancer, maternal morbidity, and end-result studies; clinicopathologic and x-ray conferences; newer diagnostic and therapeutic procedures; preoperative and postoperative supportive treatment; anesthesia; and reconditioning. Those interested in operative clinics will have an opportunity to observe newer techniques and surgical procedures. A series of exhibits demonstrating the work of the medical schools and their affiliated hospitals will be available for study in the local hospitals during the meeting, and the basic science departments of the medical schools will present graphic descriptions of their work.

The program of each hospital will be arranged to cover subjects in general surgery, obstetrics and gynecology, fractures, orthopedic surgery, thoracic surgery, neurosurgery, genitourinary surgery, ophthalmology, and otolaryngology. A daily clinical bulletin will be published to show the presentation of subjects under these classifications so that the visiting surgeon may select the programs which he wishes to attend.

CONVOCATION AND PRESIDENTIAL MEETING

The opening evening session of the Clinical Congress will be devoted to the combined presidential meeting and convocation. Since the last Congress in 1941, a total of 2,744 surgeons have been received into fellowship *in absentia*, and to them in particular the Convocation on the opening night of the Congress will be a long anticipated event. Many of these new Fellows have been

serving with the armed forces. The formal initiation ceremonies, always impressive, will be exceptionally so this year because of the large number of new Fellows accepted during the past four years who are expected to be present, in addition to the 1946 group of initiates.

Officers, Regents, and Governors have remained in office since 1941 because of the cancellation of annual meetings of the Fellows and Governors. Especial interest will also therefore be attached to the installation of the officers-elect, consisting of Dr. Irvin Abell of Louisville, chairman of the Board of Regents, as president; Dr. Leland S. McKittrick of Boston, as first vice president; and Dr. F. Phinizy Calhoun of Atlanta as second vice president.

Dr. W. Edward Gallie of Toronto, who has been president since November, 1941, will give the Presidential Address.

SCIENTIFIC SESSIONS

The scientific sessions, to be held on Tuesday, Wednesday, and Thursday evenings, will be addressed by eminent surgeons and specialists, recognized as authorities in their fields. Special scientific meetings will be arranged on the same evenings for specialists in ophthalmology and otolaryngology. The newest developments in general and special fields will be presented in the well rounded program for these evening sessions.

Every afternoon, from Monday through Thursday, panel discussions led by recognized authorities in each field, aided by well qualified collaborators, will be held. Similar meetings held during past Congresses have been most successful, largely because of the fact that they permit the participation of a large number of surgeons, thus increasing the opportunities to learn from the experiences of others.

Preliminary plans include the holding of a symposium on fractures and other traumas, on one afternoon, and a symposium on cancer on another afternoon. There is always wide interest in these special meetings. Plans for several new features have been discussed but cannot be announced until definite decisions have been made in co-operation with the Committee on Arrangements.

FORUMS ON FUNDAMENTAL SURGICAL PROBLEMS

Great interest has already been shown in the plans for reviving the Forums on Fundamental Surgical Problems which were so popular at the Boston meeting. Research activities have been retarded, but not stopped, during the war period. and the accumulation of the results of five years of work since the last Congress will certainly assure the presentation of intensely interesting material. The plan is to conduct these forums on Tuesday, Wednesday, Thursday, and Friday mornings, and to include in them brief reports of original clinical and experimental observations relating to the broad aspects of surgery and surgical specialties. No prepared discussions are planned but questions and comments will be invited. The enlistment of the interest of young men who are doing original work, through these forums, is one of the most beneficial results of these sessions which are now considered to be an indispensable feature of every Clinical Congress.

MEDICAL MOTION PICTURES

Medical motion picture exhibits will again be an appreciated feature of the Clinical Congress. The latest available pictures showing surgical procedures and related subjects will be shown. The accumulation of such pictures during the war has not been great but nevertheless a surprising number of new films are being received for review by the College and an interesting variety of educational pictures is assured. The schedule will be arranged so as not to conflict with either the clinical program at the hospitals or the scientific sessions. Both sound and silent, standard and color films, will be shown, all of which have been approved by the Committee on Medical Motion Pictures.

HOSPITAL CONFERENCES

The first formal session of the Clinical Congress will be the opening meeting of the twenty-fifth Hospital Standardization Conference. Dr. W. Edward Gallie of Toronto, president of the College, will preside. The hospital conferences will continue on Monday afternoon, with sessions following on Tuesday, Wednesday, and Thursday mornings, afternoons, and evenings.

Hospital administrators, members of governing boards, heads of the various hospital departments and their personnel, nursing groups, and many other persons directly or indirectly concerned about hospital progress, will be interested in the discussions of current hospital problems. National organizations representing various groups of hospital personnel will co-operate and participate in the meetings, which will include formal sessions, panel discussions, round table conferences, and open forums.

ADVANCE REGISTRATION

The hospitals and medical schools of New York City afford accommodations for a large number of

visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the clinics. The limit of attendance will be based on a survey determining the available facilities in the participating hospitals and schools. It is therefore expected that surgeons who wish to attend the Congress will register in advance.

In accordance with a resolution adopted by the Board of Regents, fellows of the College whose dues are paid to December 31, 1946, initiates of the classes of 1942, 1943, 1944, 1945, and 1946, and fellows in military service will not be required to pay a registration fee for the 1946 Clinical Congress. For endorsed junior candidates the fee is $5.00. Surgeons, not fellows, who attend as invited guests of the College, will pay a registration fee of $10.00.

For purposes of identification at the registration desk, fellows should present their fellowship cards. Those surgeons who pay the registration fee in advance will receive a formal receipt which they will exchange for a general admission card upon presentation at the registration desk in the Waldorf-Astoria Hotel.

HEADQUARTERS AND TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Waldorf-Astoria where there are excellent facilities. The Technical Exhibition will be held on the Third Floor near the Grand Ballroom. Leading manufacturers of surgical instruments and supplies, sutures, dressings, pharmaceuticals, operating room equipment, x-ray apparatus, hospital equipment of all kinds, and publishers of medical books will be represented in the exhibition, which will provide visiting surgeons and hospital people opportunities to inspect carefully the newest and best products of all those industries which are helping to improve the service of hospitals and surgeons.

NEW YORK HOTELS AND THEIR RATES

Besides the Waldorf-Astoria, there are a number of first class hotels which are conveniently located. In view of the extreme shortage of hotel rooms which is expected still to prevail next September, it is urged that reservations be made as soon as possible. The hotels which are recommended by the Committee appear in the following list:

	Minimum Rates with Bath	
	Single	Double
Allerton House, 143 East 39th Street	$2.75	$
Allerton House for Women, 130 East 57th Street	3.00	
Ambassador, Park Avenue & 51st Street	6.00	
Astor, Broadway & 44th Street	3.50	4.00
Barbizon (Women), Lexington Ave. & 63rd Street	3.50	
Barclay, 111 East 48th Street	6.00	8.00
Belmont Plaza, Lexington Ave. & 49th Street	4.00	6.00
Beverly, Lexington Ave. & 50th Street	5.00	
Biltmore, Madison Ave. & 43rd Street	5.50	7.50
Bristol, 129 West 48th Street	2.50	3.50
Capitol, 51st Street & 8th Avenue	3.00	4.50
Carlyle, Madison Ave. at 76th Street	6.00	
Chesterfield, 130 West 49th Street	2.50	4.00
Commodore, Lexington Ave. & 42nd Street	3.50	5.50
Concourse Plaza, Grand Concourse & 161st Street	3.50	5.50
Cornish Arms, 311 West 23rd Street	2.25	4.00
Delmonico, 502 Park Avenue	6.00	8.00
Essex House, 160 Central Park South	6.00	8.00
Fifth Avenue Hotel, 24 Fifth Ave. (9th Street)	4.00	6.00
Governor Clinton, 31st Street & 7th Ave.	3.30	4.40
Henry Hudson, 353 West 57th Street	2.50	3.50
Kenmore Hall, 145 East 23rd Street	2.00	3.50
Lexington, 48th Street & Lexington Ave.	4.00	6.00
Luxor Baths Hotel, 121 West 46th Street	2.25	
McAlpin, Broadway & 34th Street	3.30	4.95
Martinique, Broadway at 32nd Street	2.75	3.85
Midston House, 22 East 38th Street	3.50	4.00
New Weston, Madison Ave. & 50th Street	4.00	7.00
New Yorker, 34th Street & 8th Avenue	3.85	5.50
Paramount, 46th Street, West of Broadway	3.00	5.00
Park Central, 7th Avenue & 55th Street	4.00	6.00
Parkside, 18 Gramercy Park South	2.75	
Pennsylvania, 7th Avenue & 33rd Street	3.85	5.50
Piccadilly, 227 West 45th Street	3.00	5.00
Plymouth, 143 West 49th Street	2.50	3.50
President, 234 West 48th Street	2.50	4.00
Prince George, 14 East 28th Street	2.50	4.00
Roosevelt, Madison Avenue & 45th St.	4.50	6.50
Shelton, 49th Street & Lexington Avenue	3.50	5.00
Taft, 7th Avenue & 50th Street	3.00	5.00
Times Square, 43rd Street & 8th Avenue	2.25	4.00
Tudor, 304 East 42nd Street	2.50	
Victoria, 7th Ave. & 51st Street	3.00	4.50
Waldorf-Astoria, 50th Street & Park Ave.	7.00	
Warwick, 54th Street at Sixth Avenue	5.00	
Wellington, 7th Avenue & 55th Street	3.00	4.50
Woodstock, 127 West 43rd Street	3.00	5.00

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